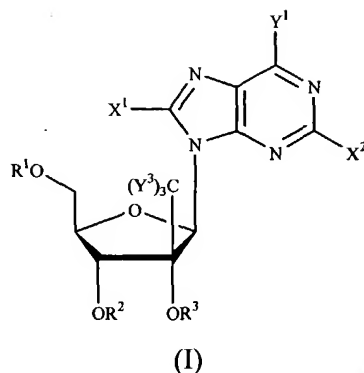


CLAIMS

What is claimed is:

1. A compound of Formula (I):



or a pharmaceutically acceptable salt thereof,

wherein:

R¹, R² and R³ are independently H; phosphate; straight chained, branched or cyclic alkyl; acyl; CO-alkyl, CO-aryl, CO-alkoxyalkyl, CO-aryloxyalkyl, CO-substituted aryl, sulfonate ester; benzyl, wherein the phenyl group is optionally substituted with one or more substituents; alkylsulfonyl; arylsulfonyl; aralkylsulfonyl; a lipid; an amino acid; an amino acid residue; a carbohydrate; a peptide; cholesterol; or pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R¹, R² and/or R³ is independently H or phosphate;

wherein at least one of R² and R³ is not hydrogen; and

wherein:

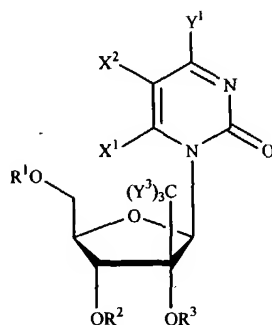
Y¹ is hydrogen, bromo, chloro, fluoro, iodo, CN, OH, OR⁴, NH₂, NHR⁴, NR⁴R⁵, SH or SR⁴;

X¹ is a straight chained, branched or cyclic optionally substituted alkyl, CH₃, CF₃, C(Y³)₃, 2-Br-ethyl, CH₂F, CH₂Cl, CH₂CF₃, CF₂CF₃, C(Y³)₂C(Y³)₃, CH₂OH, optionally substituted alkenyl, optionally substituted alkynyl, COOH, COOR⁴, COO-alkyl, COO-aryl, CO-Oalkoxyalkyl, CONH₂, CONHR⁴, CON(R⁴)₂, chloro, bromo, fluoro, iodo, CN, N₃, OH, OR⁴, NH₂, NHR⁴, NR⁴R⁵, SH or SR⁵; and

X² is H, straight chained, branched or cyclic optionally substituted alkyl, CH₃, CF₃, C(Y³)₃, 2-Br-ethyl, CH₂F, CH₂Cl, CH₂CF₃, CF₂CF₃, C(Y³)₂C(Y³)₃, CH₂OH, optionally substituted alkenyl, optionally substituted alkynyl, COOH, COOR⁴, COO-alkyl, COO-aryl, CO-Oalkoxyalkyl, CONH₂, CONHR⁴, CON(R⁴)₂, chloro, bromo, fluoro, iodo, CN, N₃, OH, OR⁴, NH₂, NHR⁴, NR⁴R⁵, SH or SR⁵; and

wherein each Y^3 is independently H, F, Cl, Br or I; and
 each R^4 and R^5 is independently hydrogen, acyl, alkyl, lower alkyl, alkenyl, alkynyl
 or cycloalkyl.

5 2. A compound of Formula (II):



(II)

or a pharmaceutically acceptable salt thereof,
 wherein:

10 R^1 , R^2 and R^3 are independently H; phosphate; straight chained, branched or cyclic
 alkyl; acyl; CO-alkyl, CO-aryl, CO-alkoxyalkyl, CO-aryloxyalkyl, CO-substituted aryl,
 sulfonate ester; benzyl, wherein the phenyl group is optionally substituted with one or more
 substituents; alkylsulfonyl; arylsulfonyl; aralkylsulfonyl; a lipid; an amino acid; an amino
 acid residue; a carbohydrate; a peptide; cholesterol; or pharmaceutically acceptable leaving
 15 group which when administered *in vivo* is capable of providing a compound wherein R^1 , R^2
 and/or R^3 is independently H or phosphate;

 wherein at least one of R^2 and R^3 is not hydrogen; and

 wherein:

Y^1 is hydrogen, bromo, chloro, fluoro, iodo, CN, OH, OR^4 , NHR^4 , NR^4R^5 , SH
 20 or SR^4 ;

X^1 is a straight chained, branched or cyclic optionally substituted alkyl, CH_3 , CF_3 ,
 $C(Y^3)_3$, 2-Br-ethyl, CH_2F , CH_2Cl , CH_2CF_3 , CF_2CF_3 , $C(Y^3)_2C(Y^3)_3$, CH_2OH , optionally
 substituted alkenyl, optionally substituted alkynyl, $COOH$, $COOR^4$, COO -alkyl, COO -aryl,
 CO -Oalkoxyalkyl, $CONH_2$, $CONHR^4$, $CON(R^4)_2$, chloro, bromo, fluoro, iodo, CN, N_3 , OH,
 25 OR^4 , NH_2 , NHR^4 , NR^4R^5 , SH or SR^5 ; and

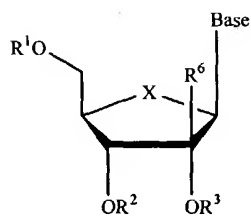
X^2 is H, straight chained, branched or cyclic optionally substituted alkyl, CH_3 , CF_3 ,
 $C(Y^3)_3$, 2-Br-ethyl, CH_2F , CH_2Cl , CH_2CF_3 , CF_2CF_3 , $C(Y^3)_2C(Y^3)_3$, CH_2OH , optionally
 substituted alkenyl, optionally substituted alkynyl, $COOH$, $COOR^4$, COO -alkyl, COO -aryl,

CO-Oalkoxyalkyl, CONH₂, CONHR⁴, CON(R⁴)₂, chloro, bromo, fluoro, iodo, CN, N₃, OH, OR⁴, NH₂, NHR⁴, NR⁴R⁵, SH or SR⁵; and

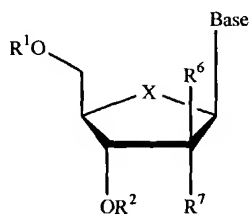
wherein each Y³ is independently H, F, Cl, Br or I; and

each R⁴ and R⁵ is independently hydrogen, acyl, alkyl, lower alkyl, alkenyl, alkynyl or cycloalkyl.

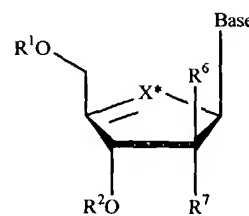
3. A compound of Formula (III), (IV) or (V):



(III)



(IV)



(V)

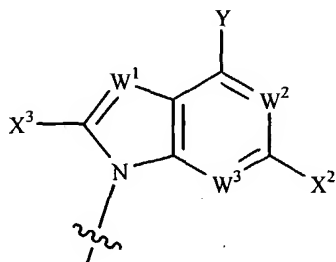
or a pharmaceutically acceptable salt thereof, wherein:

R¹, R² and R³ are independently H; phosphate; straight chained, branched or cyclic alkyl; acyl; CO-alkyl, CO-aryl, CO-alkoxyalkyl, CO-aryloxyalkyl, CO-substituted aryl, sulfonate ester; benzyl, wherein the phenyl group is optionally substituted with one or more substituents; alkylsulfonyl; arylsulfonyl; aralkylsulfonyl; a lipid; an amino acid; an amino acid residue; a carbohydrate; a peptide; cholesterol; or pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R¹, R² and/or R³ is independently H or phosphate;

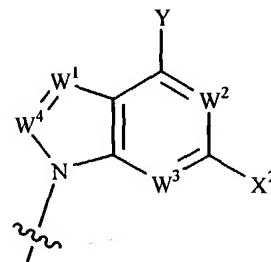
wherein at least one of R² and R³ is not hydrogen; and

wherein:

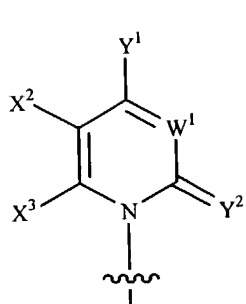
Base is selected from the group consisting of



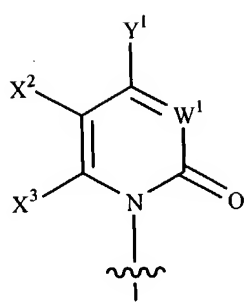
(A)



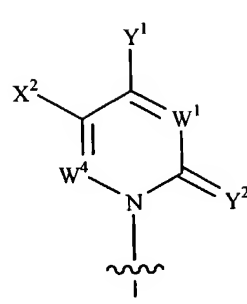
(B)



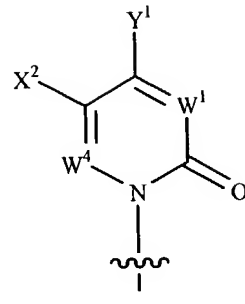
(C)



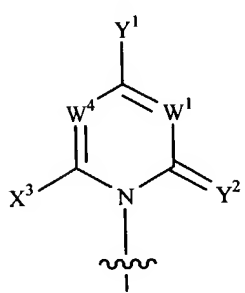
(D)



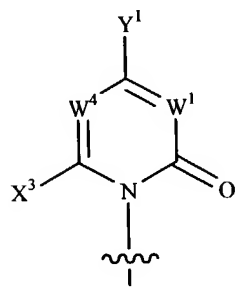
(E)



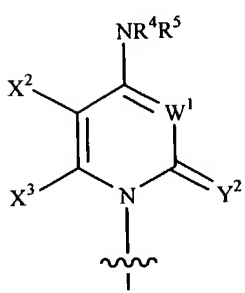
(F)



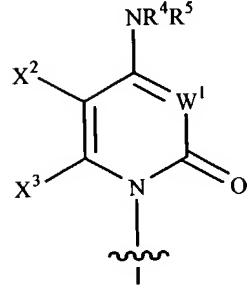
(G)



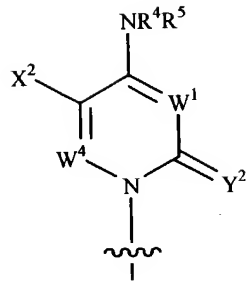
(H)



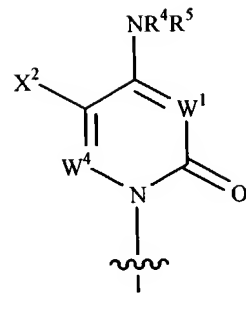
(I)



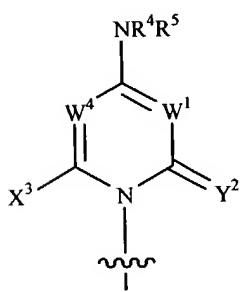
(J)



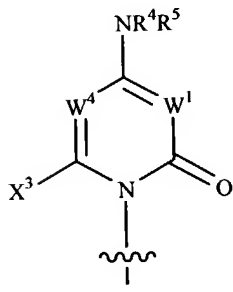
(K)



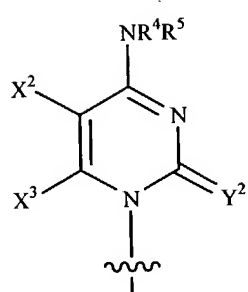
(L)



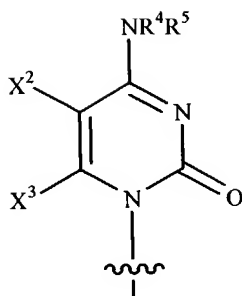
(M)



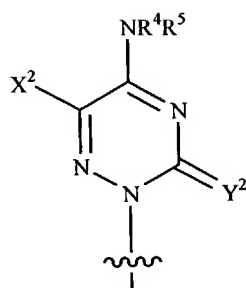
(N)



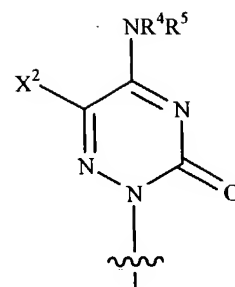
(O)



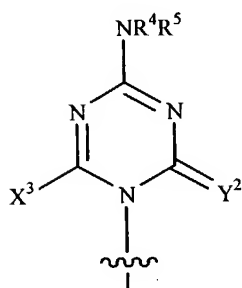
(P)



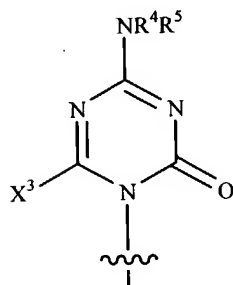
(Q)



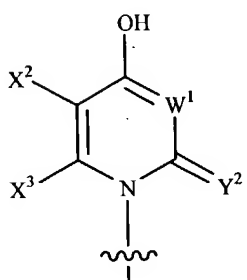
(R)



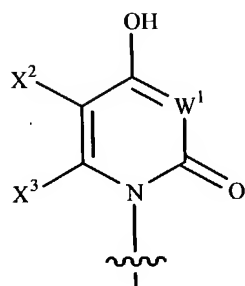
(S)



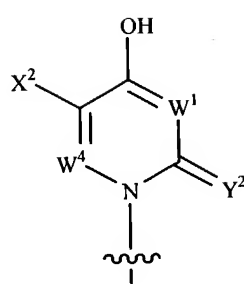
(T)



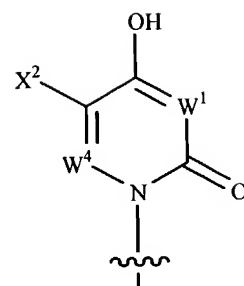
(U)



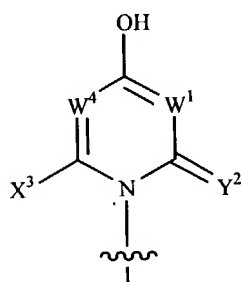
(V)



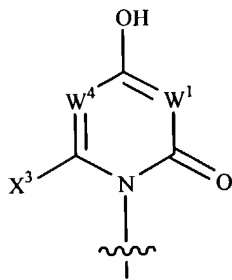
(W)



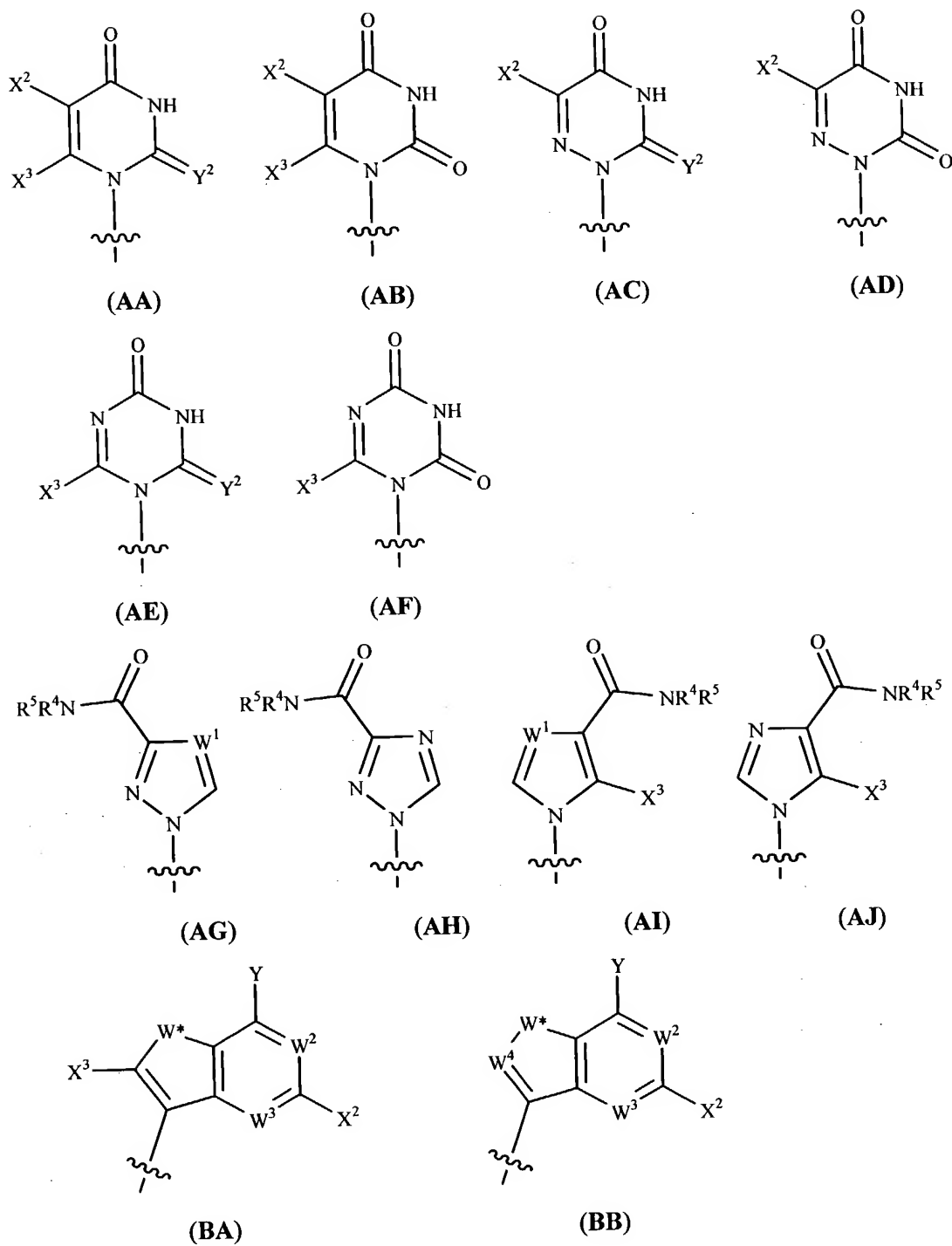
(X)

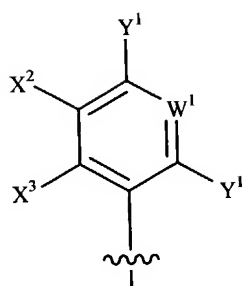


(Y)

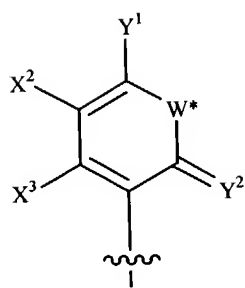


(Z)

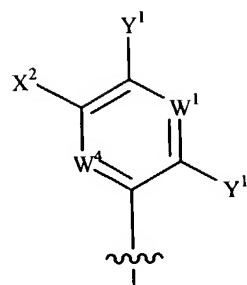




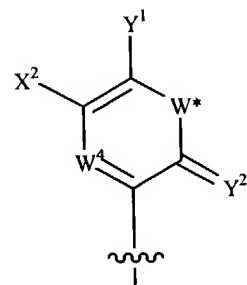
(BC)



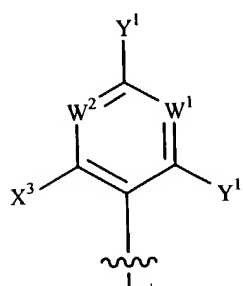
(BD)



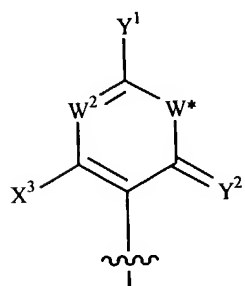
(BE)



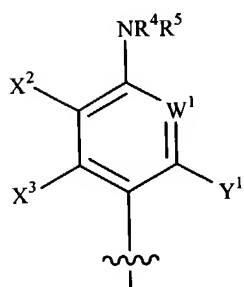
(BF)



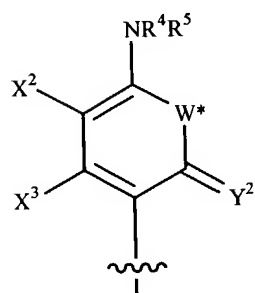
(BG)



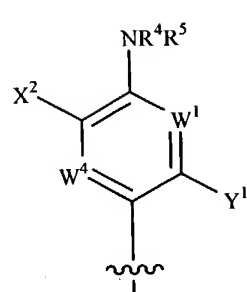
(BH)



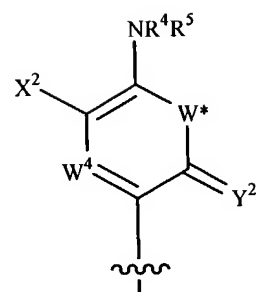
(BI)



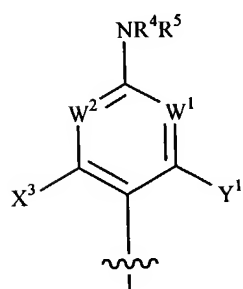
(BJ)



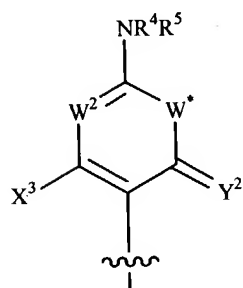
(BK)



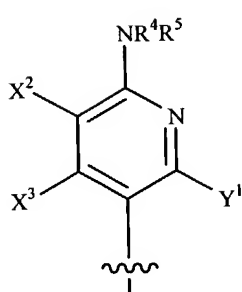
(BL)



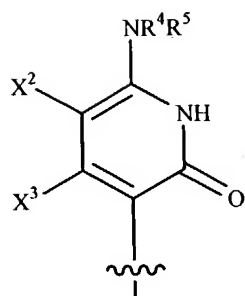
(BM)



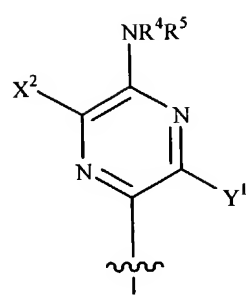
(BN)



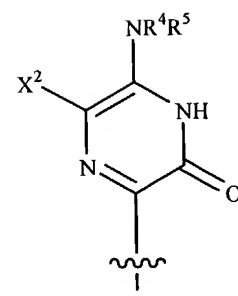
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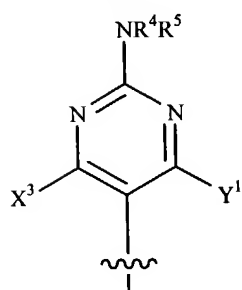
(BP)



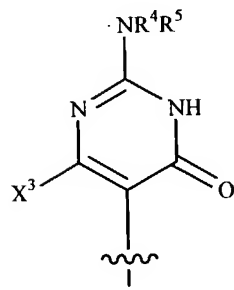
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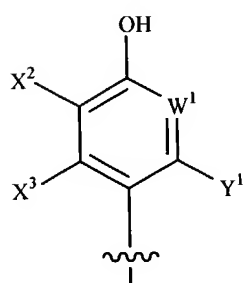
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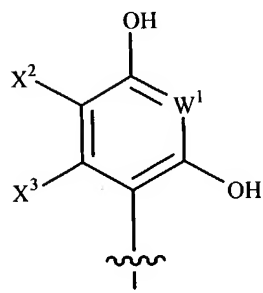
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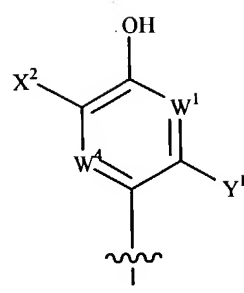
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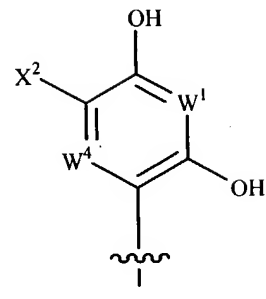
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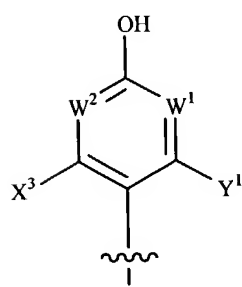
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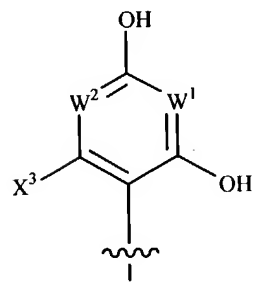
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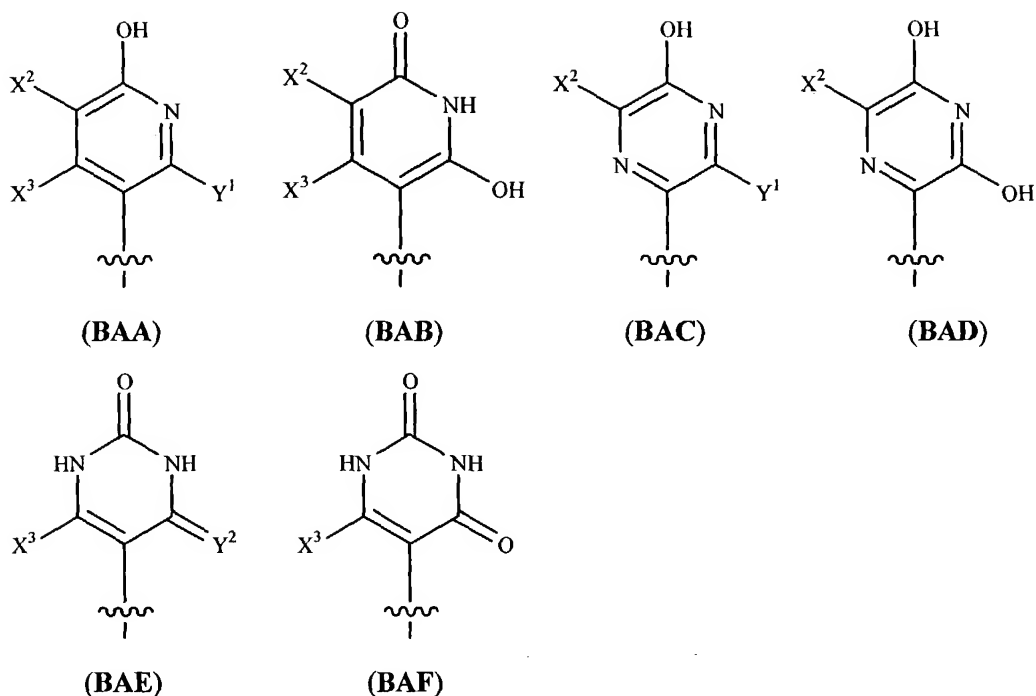
(BX)



(BY)



(BZ)



5

each R^4 and R^5 is independently hydrogen, acyl, alkyl, lower alkyl, alkenyl, alkynyl or cycloalkyl;

each W^1 , W^2 , W^3 and W^4 is independently N, CH, CF, Cl, CBr, CCl, CCN, CCH₃, CCF₃, CCH₂CH₃, CC(O)NH₂, CC(O)NHR⁴, CC(O)N(R⁴)₂, CC(O)OH, CC(O)OR⁴ or CX³;

10 each W^* is independently O, S, NH or NR⁴;

X is O, S, SO₂, CH₂, CH₂OH, CHF, CF₂, C(Y³)₂, CHCN, C(CN)₂, CHR⁴ or C(R⁴)₂;

X* is CH, CF, CY³ or CR⁴;

15 X² is H, straight chained, branched or cyclic optionally substituted alkyl, CH₃, CF₃, C(Y³)₃, 2-Br-ethyl, CH₂F, CH₂Cl, CH₂CF₃, CF₂CF₃, C(Y³)₂C(Y³)₃, CH₂OH, optionally substituted alkenyl, optionally substituted alkynyl, COOH, COOR⁴, COO-alkyl, COO-aryl, CO-Oalkoxyalkyl, CONH₂, CONHR⁴, CON(R⁴)₂, chloro, bromo, fluoro, iodo, CN, N₃, OH, OR⁴, NH₂, NHR⁴, NR⁴R⁵, SH or SR⁵;

20 each X³ is independently a straight chained, branched or cyclic optionally substituted alkyl, CH₃, CH₂CN, CH₂N₃, CH₂NH₂, CH₂NHCH₃, CH₂N(CH₃)₂, CH₂OH, halogenated alkyl, CF₃, C(Y³)₃, 2-Br-ethyl, CH₂F, CH₂Cl, CH₂CF₃, CF₂CF₃, C(Y³)₂C(Y³)₃, optionally substituted alkenyl, haloalkenyl, Br-vinyl, optionally substituted alkynyl, haloalkynyl, N₃, CN, -C(O)OH, -C(O)OR⁴, -C(O)O(lower alkyl), -C(O)NH₂, -C(O)NHR⁴, -C(O)NH(lower alkyl), -C(O)N(R⁴)₂, -C(O)N(lower alkyl)₂, OH, OR⁴, -O(acyl), -O(lower

acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), -O(alkynyl), -O(aralkyl), -O(cycloalkyl), -S(acyl), -S(lower acyl), -S(R⁴), -S(lower alkyl), -S(alkenyl), -S(alkynyl), -S(aralkyl), -S(cycloalkyl), chloro, bromo, fluoro, iodo, NH₂, -NH(lower alkyl), -NHR⁴, -NR⁴R⁵, -NH(acyl), -N(lower alkyl)₂, -NH(alkenyl), -NH(alkynyl), -NH(aralkyl), -NH(cycloalkyl), or -N(acyl)₂;

each Y is independently selected from the group consisting of H, optionally substituted lower alkyl, cycloalkyl, alkenyl, alkynyl, CH₂OH, CH₂NH₂, CH₂NHCH₃, CH₂N(CH₃)₂, CH₂F, CH₂Cl, CH₂N₃, CH₂CN, CH₂CF₃, CF₃, CF₂CF₃, CH₂CO₂R, (CH₂)_mCOOH, (CH₂)_mCOOR, (CH₂)_mCONH₂, (CH₂)_mCONR₂, and (CH₂)_mCONHR;

R is H, alkyl or acyl;

Y¹ is hydrogen, bromo, chloro, fluoro, iodo, CN, OH, OR⁴, NH₂, NHR⁴, NR⁴R⁵, SH or SR⁴;

each Y² is independently O, S, NH or NR⁴; and

each Y³ is independently H, F, Cl, Br or I;

wherein for Base (B), W⁴ cannot be CH if W¹, W² and W³ are N;

wherein for Base (E), (F), (K), (L), (W) and (X), W⁴ cannot be CH if W¹ is N;

each R⁶ is independently an optionally substituted alkyl, CH₃, CH₂CN, CH₂N₃, CH₂NH₂, CH₂NHCH₃, CH₂N(CH₃)₂, CH₂OH, halogenated alkyl, CF₃, C(Y³)₃, 2-Br-ethyl, CH₂F, CH₂Cl, CH₂CF₃, CF₂CF₃, C(Y³)₂C(Y³)₃, optionally substituted alkenyl, haloalkenyl, Br-vinyl, optionally substituted alkynyl, haloalkynyl, -CH₂C(O)OH, -CH₂C(O)OR⁴, -CH₂C(O)O(lower alkyl), -CH₂C(O)NH₂, -CH₂C(O)NHR⁴, -CH₂C(O)NH(lower alkyl), -CH₂C(O)N(R⁴)₂, -CH₂C(O)N(lower alkyl)₂, -(CH₂)_mC(O)OH, -(CH₂)_mC(O)OR⁴, -(CH₂)_mC(O)O(lower alkyl), -(CH₂)_mC(O)NH₂, -(CH₂)_mC(O)NHR⁴, -(CH₂)_mC(O)NH(lower alkyl), -(CH₂)_mC(O)N(R⁴)₂, -(CH₂)_mC(O)N(lower alkyl)₂, -C(O)OH, -C(O)OR⁴, -C(O)O(lower alkyl), -C(O)NH₂, -C(O)NHR⁴, -C(O)NH(lower alkyl), -C(O)N(R⁴)₂, -C(O)N(lower alkyl)₂ or cyano;

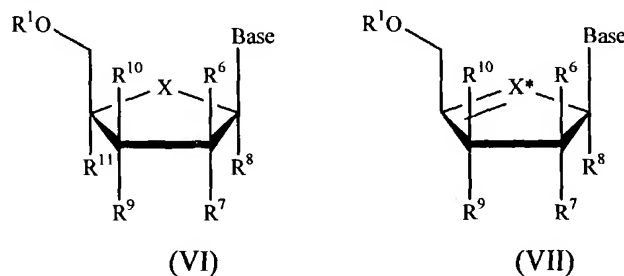
each R⁷ is independently OH, OR², optionally substituted alkyl, CH₃, CH₂CN, CH₂N₃, CH₂NH₂, CH₂NHCH₃, CH₂N(CH₃)₂, CH₂OH, halogenated alkyl, CF₃, C(Y³)₃, 2-Br-ethyl, CH₂F, CH₂Cl, CH₂CF₃, CF₂CF₃, C(Y³)₂C(Y³)₃, optionally substituted alkenyl, haloalkenyl, Br-vinyl, optionally substituted alkynyl, haloalkynyl, optionally substituted carbocycle, optionally substituted heterocycle, optionally substituted heteroaryl, -CH₂C(O)OH, -CH₂C(O)OR⁴, -CH₂C(O)O(lower alkyl), -CH₂C(O)SH, -CH₂C(O)SR⁴, -CH₂C(O)S(lower alkyl), -CH₂C(O)NH₂, -CH₂C(O)NHR⁴, -CH₂C(O)NH(lower alkyl), -CH₂C(O)N(R⁴)₂, -CH₂C(O)N(lower alkyl)₂, -(CH₂)_mC(O)OH, -(CH₂)_mC(O)OR⁴,

$-(CH_2)_mC(O)O(\text{lower alkyl})$, $-(CH_2)_mC(O)SH$, $-(CH_2)_mC(O)SR^4$, $-(CH_2)_mC(O)S(\text{lower alkyl})$, $-(CH_2)_mC(O)NH_2$, $-(CH_2)_mC(O)NHR^4$, $-(CH_2)_mC(O)NH(\text{lower alkyl})$, $-(CH_2)_mC(O)N(R^4)_2$, $-(CH_2)_mC(O)N(\text{lower alkyl})_2$, $-C(O)OH$, $-C(O)OR^4$, $-C(O)O(\text{lower alkyl})$, $-C(O)SH$, $-C(O)SR^4$, $-C(O)S(\text{lower alkyl})$, $-C(O)NH_2$, $-C(O)NHR^4$, $-C(O)NH(\text{lower alkyl})$, $-C(O)N(R^4)_2$, $-C(O)N(\text{lower alkyl})_2$, $-O(\text{acyl})$, $-O(\text{lower acyl})$, $-O(R^4)$, $-O(\text{alkyl})$, $-O(\text{lower alkyl})$, $-O(\text{alkenyl})$, $-O(\text{alkynyl})$, $-O(\text{aralkyl})$, $-O(\text{cycloalkyl})$, $-S(\text{acyl})$, $-S(\text{lower acyl})$, $-S(R^4)$, $-S(\text{lower alkyl})$, $-S(\text{alkenyl})$, $-S(\text{alkynyl})$, $-S(\text{aralkyl})$, $-S(\text{cycloalkyl})$, NO_2 , NH_2 , $-NH(\text{lower alkyl})$, $-NHR^4$, $-NR^4R^5$, $-NH(\text{acyl})$, $-N(\text{lower alkyl})_2$, $-NH(\text{alkenyl})$, $-NH(\text{alkynyl})$, $-NH(\text{aralkyl})$, $-NH(\text{cycloalkyl})$, $-N(\text{acyl})_2$, azido, cyano, SCN, OCN, NCO or halo;

alternatively, R^6 and R^7 can come together to form a spiro compound selected from the group consisting of optionally substituted carbocycle or optionally substituted heterocycle; and

each m is independently 0, 1 or 2.

4. A compound of Formula (VI) or (VII):



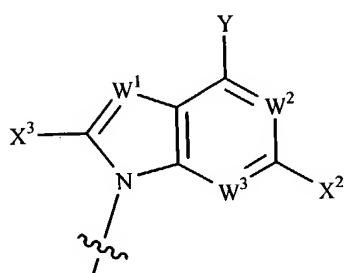
or a pharmaceutically acceptable salt thereof,

wherein:

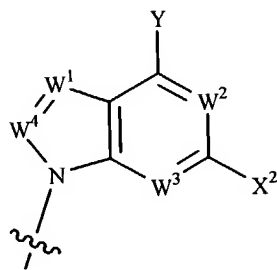
R^1 is H; phosphate; straight chained, branched or cyclic alkyl; acyl; CO-alkyl; CO-aryl; CO-alkoxyalkyl; CO-aryloxyalkyl; CO-substituted aryl; sulfonate ester; benzyl, wherein the phenyl group is optionally substituted with one or more substituents; alkylsulfonyl; arylsulfonyl; aralkylsulfonyl; a lipid; an amino acid; an amino acid residue; a carbohydrate; a peptide; cholesterol; or pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1 is H or phosphate; and

wherein:

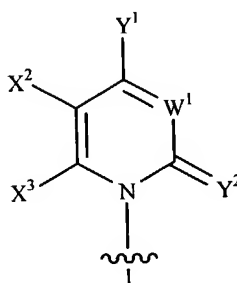
Base is selected from the group consisting of



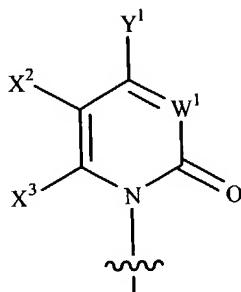
(A)



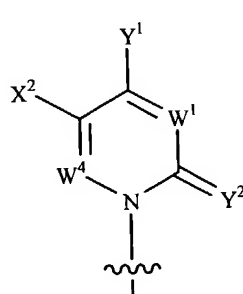
(B)



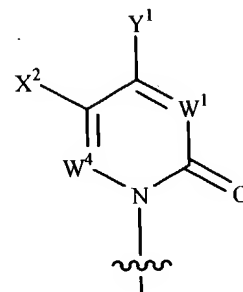
(C)



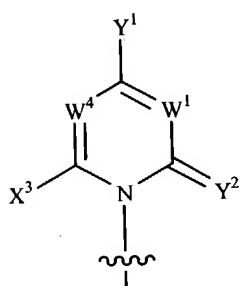
(D)



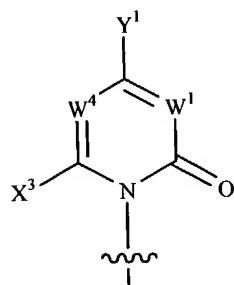
(E)



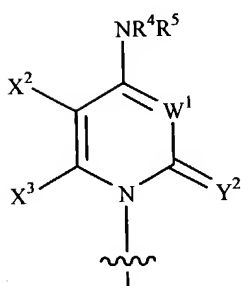
(F)



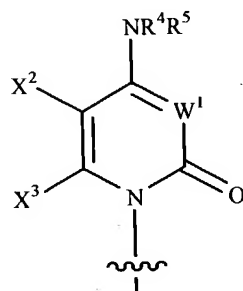
(G)



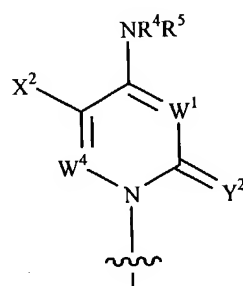
(H)



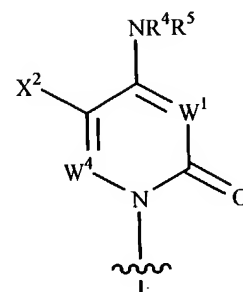
(I)



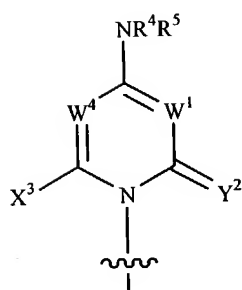
(J)



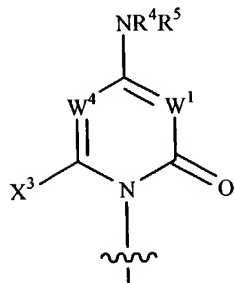
(K)



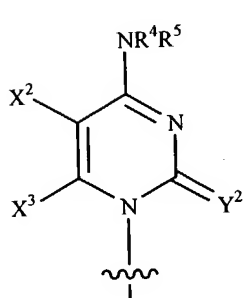
(L)



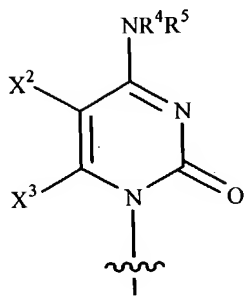
(M)



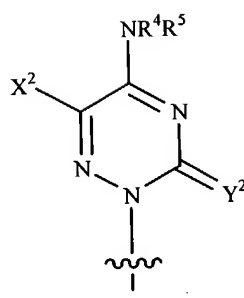
(N)



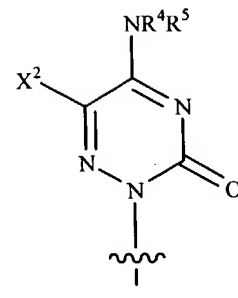
(O)



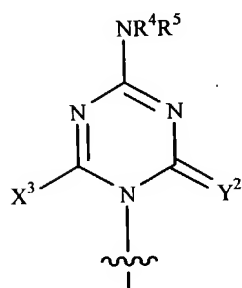
(P)



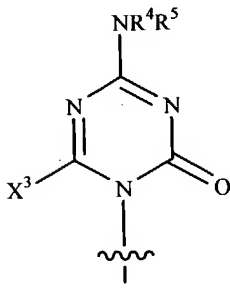
(Q)



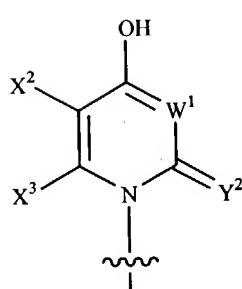
(R)



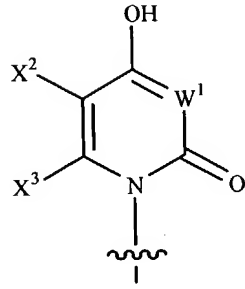
(S)



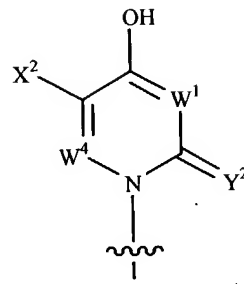
(T)



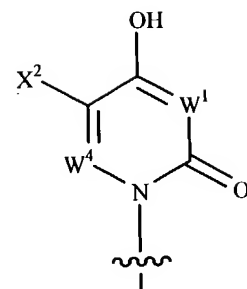
(U)



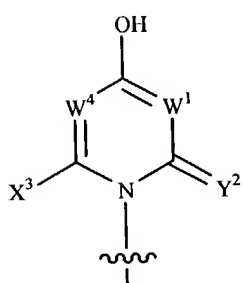
(V)



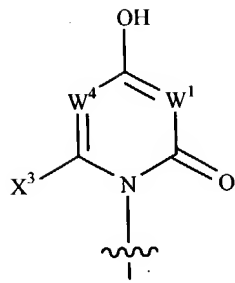
(W)



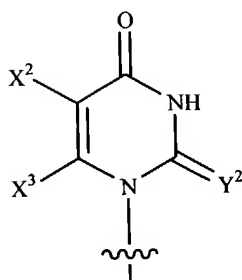
(X)



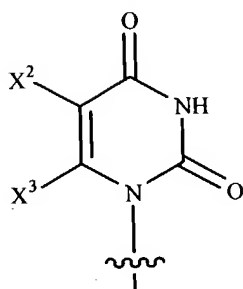
(Y)



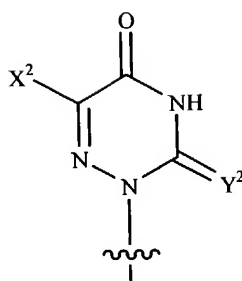
(Z)



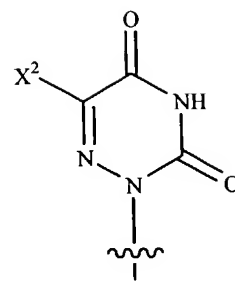
(AA)



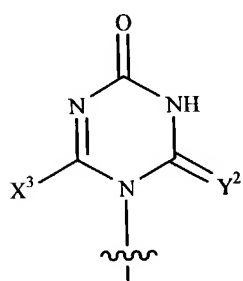
(AB)



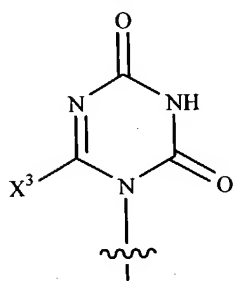
(AC)



(AD)

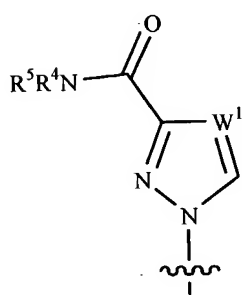


(AE)

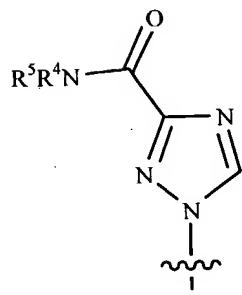


(AF)

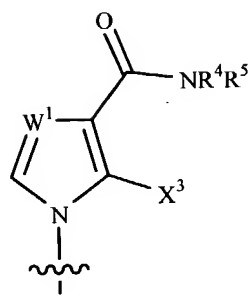
5



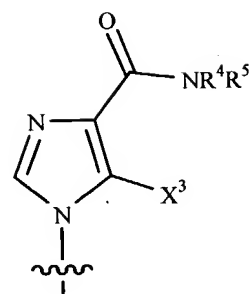
(AG)



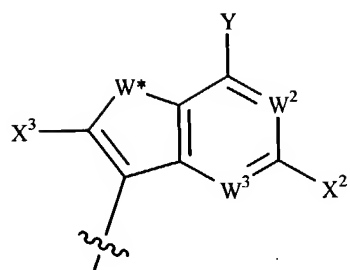
(AH)



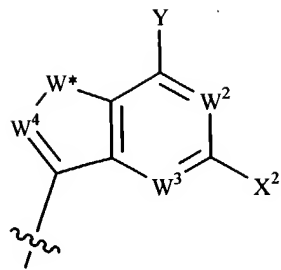
(AI)



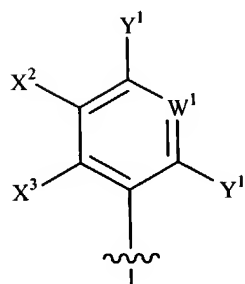
(AJ)



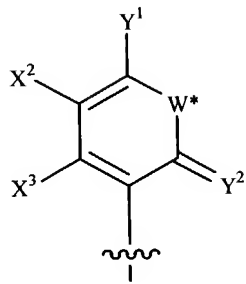
(BA)



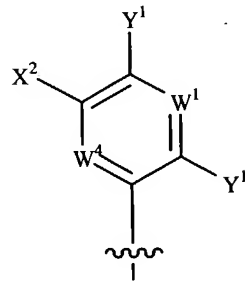
(BB)



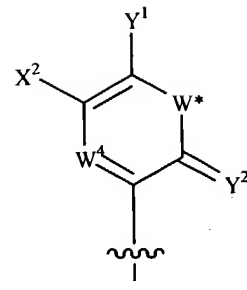
(BC)



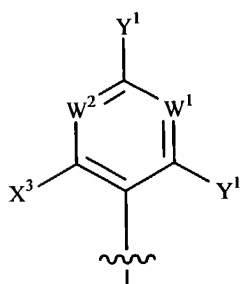
(BD)



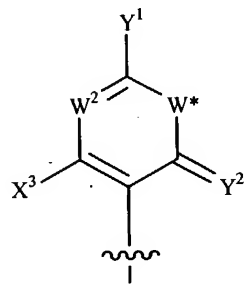
(BE)



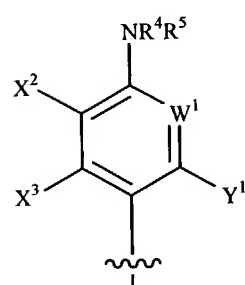
(BF)



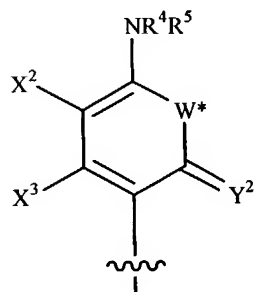
(BG)



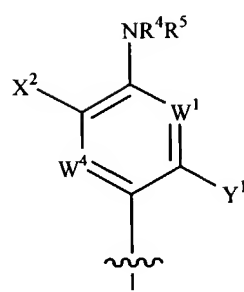
(BH)



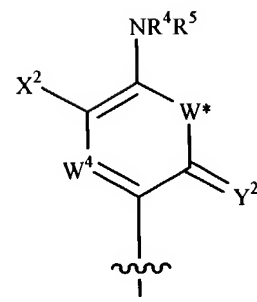
(BI)



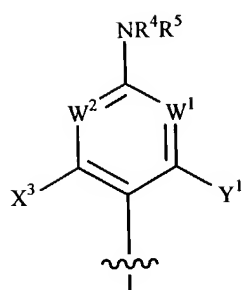
(BJ)



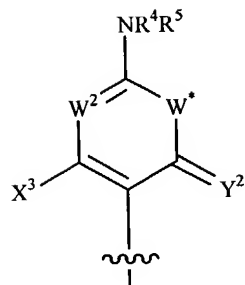
(BK)



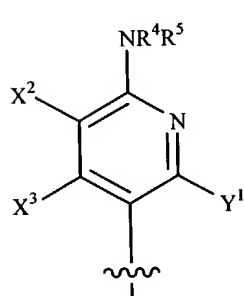
(BL)



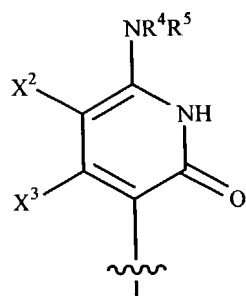
(BM)



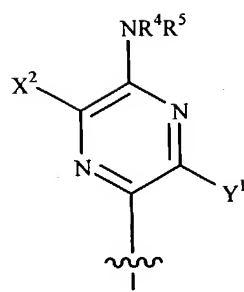
(BN)



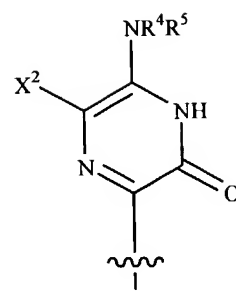
(BO)



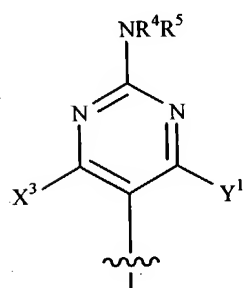
(BP)



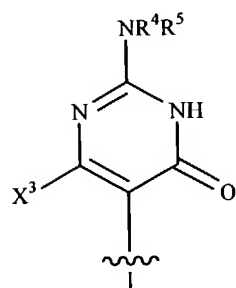
(BQ)



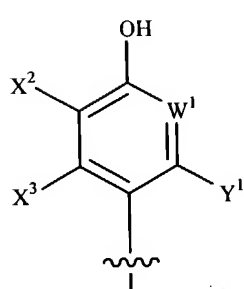
(BR)



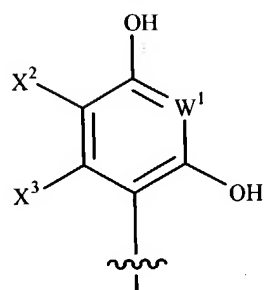
(BS)



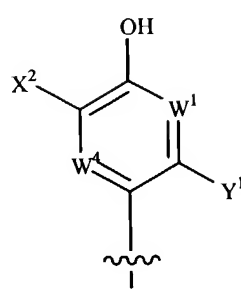
(BT)



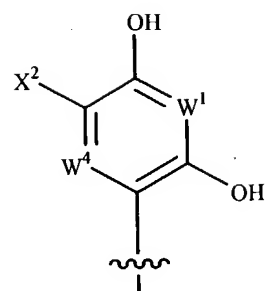
(BU)



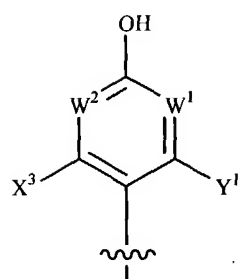
(BV)



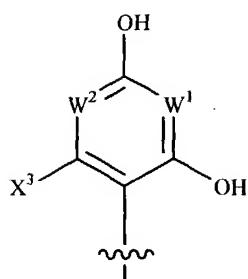
(BW)



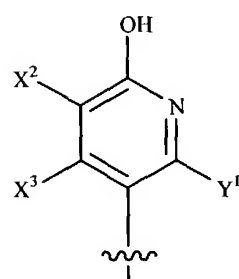
(BX)



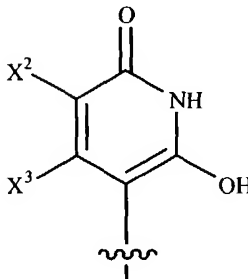
(BY)



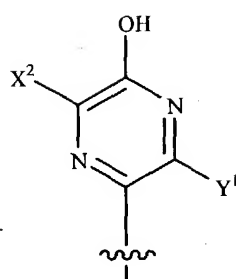
(BZ)



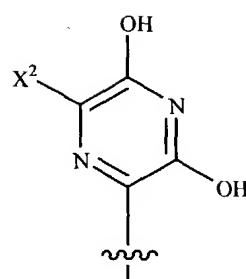
(BAA)



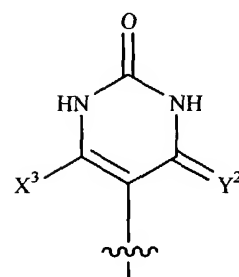
(BAB)



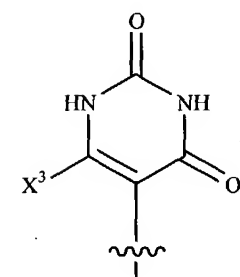
(BAC)



(BAD)



(BAE)



(BAF)

5

each R^4 and R^5 is independently hydrogen, acyl, alkyl, lower alkyl, alkenyl, alkynyl or cycloalkyl;

10

each W^1 , W^2 , W^3 and W^4 is independently N, CH, CF, Cl, CBr, CCl, CCN, CCH₃, CCF₃, CCH₂CH₃, CC(O)NH₂, CC(O)NHR⁴, CC(O)N(R⁴)₂, CC(O)OH, CC(O)OR⁴ or CX³;

each W^* is independently O, S, NH or NR⁴;

X is O, S, SO₂, CH₂, CH₂OH, CHF, CF₂, C(Y³)₂, CHCN, C(CN)₂, CHR⁴ or C(R⁴)₂;

X* is CH, CF, CY³ or CR⁴;

15

X² is H, straight chained, branched or cyclic optionally substituted alkyl, CH₃, CF₃, C(Y³)₃, 2-Br-ethyl, CH₂F, CH₂Cl, CH₂CF₃, CF₂CF₃, C(Y³)₂C(Y³)₃, CH₂OH, optionally substituted alkenyl, optionally substituted alkynyl, COOH, COOR⁴, COO-alkyl, COO-aryl,

CO-Oalkoxyalkyl, CONH₂, CONHR⁴, CON(R⁴)₂, chloro, bromo, fluoro, iodo, CN, N₃, OH, OR⁴, NH₂, NHR⁴, NR⁴R⁵, SH or SR⁵;

each X³ is independently a straight chained, branched or cyclic optionally substituted alkyl, CH₃, CH₂CN, CH₂N₃, CH₂NH₂, CH₂NHCH₃, CH₂N(CH₃)₂, CH₂OH, halogenated alkyl, CF₃, C(Y³)₃, 2-Br-ethyl, CH₂F, CH₂Cl, CH₂CF₃, CF₂CF₃, C(Y³)₂C(Y³)₃, optionally substituted alkenyl, haloalkenyl, Br-vinyl, optionally substituted alkynyl, haloalkynyl, N₃, CN, -C(O)OH, -C(O)OR⁴, -C(O)O(lower alkyl), -C(O)NH₂, -C(O)NHR⁴, -C(O)NH(lower alkyl), -C(O)N(R⁴)₂, -C(O)N(lower alkyl)₂, OH, OR⁴, -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), -O(alkynyl), -O(aralkyl), -O(cycloalkyl), -S(acyl), -S(lower acyl), -S(R⁴), -S(lower alkyl), -S(alkenyl), -S(alkynyl), -S(aralkyl), -S(cycloalkyl), chloro, bromo, fluoro, iodo, NH₂, -NH(lower alkyl), -NHR⁴, -NR⁴R⁵, -NH(acyl), -N(lower alkyl)₂, -NH(alkenyl), -NH(alkynyl), -NH(aralkyl), -NH(cycloalkyl), or -N(acyl)₂;

each Y is independently selected from the group consisting of H, optionally substituted lower alkyl, cycloalkyl, alkenyl, alkynyl, CH₂OH, CH₂NH₂, CH₂NHCH₃, CH₂N(CH₃)₂, CH₂F, CH₂Cl, CH₂N₃, CH₂CN, CH₂CF₃, CF₃, CF₂CF₃, CH₂CO₂R, (CH₂)_mCOOH, (CH₂)_mCOOR, (CH₂)_mCONH₂, (CH₂)_mCONR₂, and (CH₂)_mCONHR;

R is H, alkyl or acyl;

Y¹ is hydrogen, bromo, chloro, fluoro, iodo, CN, OH, OR⁴, NH₂, NHR⁴, NR⁴R⁵, SH or SR⁴;

each Y² is independently O, S, NH or NR⁴;

each Y³ is independently H, F, Cl, Br or I;

wherein for Base (B), W⁴ cannot be CH if W¹, W² and W³ are N;

wherein for Base (E), (F), (K), (L), (W) and (X), W⁴ cannot be CH if W¹ is N;

each R⁶ is independently an optionally substituted alkyl, CH₃, CH₂CN, CH₂N₃, CH₂NH₂, CH₂NHCH₃, CH₂N(CH₃)₂, CH₂OH, halogenated alkyl, CF₃, C(Y³)₃, 2-Br-ethyl, CH₂F, CH₂Cl, CH₂CF₃, CF₂CF₃, C(Y³)₂C(Y³)₃, optionally substituted alkenyl, haloalkenyl, Br-vinyl, optionally substituted alkynyl, haloalkynyl, -CH₂C(O)OH, -CH₂C(O)OR⁴, -CH₂C(O)O(lower alkyl), -CH₂C(O)NH₂, -CH₂C(O)NHR⁴, -CH₂C(O)NH(lower alkyl), -CH₂C(O)N(R⁴)₂, -CH₂C(O)N(lower alkyl)₂, -(CH₂)_mC(O)OH, -(CH₂)_mC(O)OR⁴, -(CH₂)_mC(O)O(lower alkyl), -(CH₂)_mC(O)NH₂, -(CH₂)_mC(O)NHR⁴, -(CH₂)_mC(O)NH(lower alkyl), -(CH₂)_mC(O)N(R⁴)₂, -(CH₂)_mC(O)N(lower alkyl)₂, -C(O)OH, -C(O)OR⁴, -C(O)O(lower alkyl), -C(O)NH₂, -C(O)NHR⁴, -C(O)NH(lower alkyl), -C(O)N(R⁴)₂, -C(O)N(lower alkyl)₂ or cyano;

each R^7 is independently OH, OR^2 , optionally substituted alkyl, CH_3 , CH_2CN , CH_2N_3 , CH_2NH_2 , CH_2NHCH_3 , $CH_2N(CH_3)_2$, CH_2OH , halogenated alkyl, CF_3 , $C(Y^3)_3$, 2-Br-ethyl, CH_2F , CH_2Cl , CH_2CF_3 , CF_2CF_3 , $C(Y^3)_2C(Y^3)_3$, optionally substituted alkenyl, haloalkenyl, Br-vinyl, optionally substituted alkynyl, haloalkynyl, optionally substituted carbocycle, optionally substituted heterocycle, optionally substituted heteroaryl,
5 - $CH_2C(O)OH$, - $CH_2C(O)OR^4$, - $CH_2C(O)O$ (lower alkyl), - $CH_2C(O)SH$, - $CH_2C(O)SR^4$,
- $CH_2C(O)S$ (lower alkyl), - $CH_2C(O)NH_2$, - $CH_2C(O)NHR^4$, - $CH_2C(O)NH$ (lower alkyl),
- $CH_2C(O)N(R^4)_2$, - $CH_2C(O)N$ (lower alkyl) $_2$, - $(CH_2)_mC(O)OH$, - $(CH_2)_mC(O)OR^4$,
- $(CH_2)_mC(O)O$ (lower alkyl), - $(CH_2)_mC(O)SH$, - $(CH_2)_mC(O)SR^4$, - $(CH_2)_mC(O)S$ (lower
10 alkyl), - $(CH_2)_mC(O)NH_2$, - $(CH_2)_mC(O)NHR^4$, - $(CH_2)_mC(O)NH$ (lower alkyl),
- $(CH_2)_mC(O)N(R^4)_2$, - $(CH_2)_mC(O)N$ (lower alkyl) $_2$, - $C(O)OH$, - $C(O)OR^4$, - $C(O)O$ (lower
alkyl), - $C(O)SH$, - $C(O)SR^4$, - $C(O)S$ (lower alkyl), - $C(O)NH_2$, - $C(O)NHR^4$, - $C(O)NH$ (lower
alkyl), - $C(O)N(R^4)_2$, - $C(O)N$ (lower alkyl) $_2$, - O (acyl), - O (lower acyl), - $O(R^4)$, - O (alkyl),
- O (lower alkyl), - O (alkenyl), - O (alkynyl), - O (aralkyl), - O (cycloalkyl), - S (acyl), - S (lower
15 acyl), - $S(R^4)$, - S (lower alkyl), - S (alkenyl), - S (alkynyl), - S (aralkyl), - S (cycloalkyl), NO_2 ,
 NH_2 , - NH (lower alkyl), - NHR^4 , - NR^4R^5 , - NH (acyl), - N (lower alkyl) $_2$, - NH (alkenyl),
- NH (alkynyl), - NH (aralkyl), - NH (cycloalkyl), - N (acyl) $_2$, azido, cyano, SCN , OCN , NCO or
halo;

alternatively, R^6 and R^7 can come together to form a spiro compound selected from
20 the group consisting of optionally substituted carbocycle or optionally substituted
heterocycle;

each R^8 and R^{11} is independently hydrogen, an optionally substituted alkyl, CH_3 ,
 CH_2CN , CH_2N_3 , CH_2NH_2 , CH_2NHCH_3 , $CH_2N(CH_3)_2$, CH_2OH , halogenated alkyl, CF_3 ,
 $C(Y^3)_3$, 2-Br-ethyl, CH_2F , CH_2Cl , CH_2CF_3 , CF_2CF_3 , $C(Y^3)_2C(Y^3)_3$, optionally substituted
25 alkenyl, haloalkenyl, Br-vinyl, optionally substituted alkynyl, haloalkynyl, - $CH_2C(O)OH$,
- $CH_2C(O)OR^4$, - $CH_2C(O)O$ (lower alkyl), - $CH_2C(O)NH_2$, - $CH_2C(O)NHR^4$,
- $CH_2C(O)NH$ (lower alkyl), - $CH_2C(O)N(R^4)_2$, - $CH_2C(O)N$ (lower alkyl) $_2$, - $(CH_2)_mC(O)OH$,
- $(CH_2)_mC(O)OR^4$, - $(CH_2)_mC(O)O$ (lower alkyl), - $(CH_2)_mC(O)NH_2$, - $(CH_2)_mC(O)NHR^4$,
- $(CH_2)_mC(O)NH$ (lower alkyl), - $(CH_2)_mC(O)N(R^4)_2$, - $(CH_2)_mC(O)N$ (lower alkyl) $_2$,
30 - $C(O)OH$, - $C(O)OR^4$, - $C(O)O$ (lower alkyl), - $C(O)NH_2$, - $C(O)NHR^4$, - $C(O)NH$ (lower alkyl),
- $C(O)N(R^4)_2$, - $C(O)N$ (lower alkyl) $_2$, cyano, NH -acyl or N (acyl) $_2$;

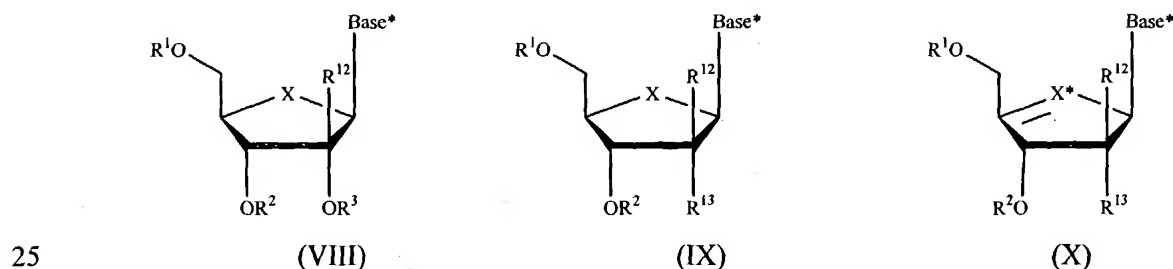
each R^9 and R^{10} are independently hydrogen, OH, OR^2 , optionally substituted alkyl,
 CH_3 , CH_2CN , CH_2N_3 , CH_2NH_2 , CH_2NHCH_3 , $CH_2N(CH_3)_2$, CH_2OH , halogenated alkyl CF_3 ,
 $C(Y^3)_3$, 2-Br-ethyl, CH_2F , CH_2Cl , CH_2CF_3 , CF_2CF_3 , $C(Y^3)_2C(Y^3)_3$, optionally substituted

alkenyl, haloalkenyl, Br-vinyl, optionally substituted alkynyl, haloalkynyl, optionally substituted carbocycle, optionally substituted heterocycle, optionally substituted heteroaryl, -CH₂C(O)OH, -CH₂C(O)OR⁴, -CH₂C(O)O(lower alkyl), -CH₂C(O)SH, -CH₂C(O)SR⁴, -CH₂C(O)S(lower alkyl), -CH₂C(O)NH₂, -CH₂C(O)NHR⁴, -CH₂C(O)NH(lower alkyl),
 5 -CH₂C(O)N(R⁴)₂, -CH₂C(O)N(lower alkyl)₂, -(CH₂)_mC(O)OH, -(CH₂)_mC(O)OR⁴, -(CH₂)_mC(O)O(lower alkyl), -(CH₂)_mC(O)SH, -(CH₂)_mC(O)SR⁴, -(CH₂)_mC(O)S(lower alkyl), -(CH₂)_mC(O)NH₂, -(CH₂)_mC(O)NHR⁴, -(CH₂)_mC(O)NH(lower alkyl), -(CH₂)_mC(O)N(R⁴)₂, -(CH₂)_mC(O)N(lower alkyl)₂, -C(O)OH, -C(O)OR⁴, -C(O)O(lower alkyl), -C(O)SH, -C(O)SR⁴, -C(O)S(lower alkyl), -C(O)NH₂, -C(O)NHR⁴, -C(O)NH(lower alkyl),
 10 -C(O)N(R⁴)₂, -C(O)N(lower alkyl)₂, -O(acyl), -O(lower acyl), -O(R⁴), -O(alkyl), -O(lower alkyl), -O(alkenyl), -O(alkynyl), -O(aralkyl), -O(cycloalkyl), -S(acyl), -S(lower acyl), -S(R⁴), -S(lower alkyl), -S(alkenyl), -S(alkynyl), -S(aralkyl), -S(cycloalkyl), NO₂, NH₂, -NH(lower alkyl), -NHR⁴, -NR⁴R⁵, -NH(acyl), -N(lower alkyl)₂, -NH(alkenyl), -NH(alkynyl), -NH(aralkyl), -NH(cycloalkyl), -N(acyl)₂, azido, cyano, SCN, OCN, NCO or halo;

each m is independently 0, 1 or 2; and

alternatively, R⁶ and R¹⁰, R⁷ and R⁹, R⁸ and R⁷ or R⁹ and R¹¹ can come together to form a bridged compound selected from the group consisting of optionally substituted carbocycle or optionally substituted heterocycle or alternatively, R⁶ and R⁷ or R⁹ and R¹⁰
 20 can come together to form a spiro compound selected from the group consisting of optionally substituted carbocycle or optionally substituted heterocycle.

5. A compound of Formula (VIII), (IX) or (X):



or a pharmaceutically acceptable salt thereof, wherein:

wherein R¹, R² and R³ are independently H; phosphate; straight chained, branched or cyclic alkyl; acyl; CO-alkyl; CO-aryl; CO-alkoxyalkyl; CO-aryloxyalkyl; CO-substituted aryl; sulfonate ester; benzyl, wherein the phenyl group is optionally substituted with one or
 30 more substituents; alkylsulfonyl; arylsulfonyl; aralkylsulfonyl; a lipid; an amino acid; an

amino acid residue; a carbohydrate; a peptide; cholesterol; or pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1 , R^2 and/or R^3 is independently H or phosphate;

wherein at least one of R^2 and R^3 is not hydrogen;

5 X is O, S, SO_2 , CH_2 , CH_2OH , CHF, CF_2 , $C(Y^3)_2$, CHCN, $C(CN)_2$, CHR^4 or $C(R^4)_2$;

X^* is CH, CF, CY^3 , or CR^4 ;

each Y^3 is independently H, F, Cl, Br or I;

each R^4 and R^5 is independently hydrogen, acyl, alkyl, lower alkyl, alkenyl or cycloalkyl;

10 Base* is a purine or pyrimidine base;

each R^{12} is independently a substituted alkyl, CH_2CN , CH_2N_3 , CH_2NH_2 ,

CH_2NHCH_3 , $CH_2N(CH_3)_2$, CH_2OH , halogenated alkyl, CF_3 , $C(Y^3)_3$, 2-Br-ethyl, CH_2F , CH_2Cl , CH_2CF_3 , CF_2CF_3 , $C(Y^3)_2C(Y^3)_3$, substituted alkenyl, haloalkenyl (but not Br-vinyl), substituted alkynyl, haloalkynyl, $-CH_2C(O)OH$, $-CH_2C(O)OR^4$, $-CH_2C(O)O$ (lower alkyl),

15 $-CH_2C(O)NH_2$, $-CH_2C(O)NHR^4$, $-CH_2C(O)NH$ (lower alkyl), $-CH_2C(O)N(R^4)_2$,

$-CH_2C(O)N$ (lower alkyl) $_2$, $-(CH_2)_mC(O)OH$, $-(CH_2)_mC(O)OR^4$, $-(CH_2)_mC(O)O$ (lower alkyl), $-(CH_2)_mC(O)NH_2$, $-(CH_2)_mC(O)NHR^4$, $-(CH_2)_mC(O)NH$ (lower alkyl),

$-(CH_2)_mC(O)N(R^4)_2$, $-(CH_2)_mC(O)N$ (lower alkyl) $_2$, $-C(O)OH$, $-C(O)OR^4$, $-C(O)NH_2$,

$-C(O)NHR^4$, $-C(O)NH$ (lower alkyl), $-C(O)N(R^4)_2$, $-C(O)N$ (lower alkyl) $_2$;

20 each R^{13} is independently substituted alkyl, CH_2CN , CH_2N_3 , CH_2NH_2 , CH_2NHCH_3 ,

$CH_2N(CH_3)_2$, CH_2OH , halogenated alkyl, CF_3 , $C(Y^3)_3$, 2-Br-ethyl, CH_2F , CH_2Cl , CH_2CF_3 , CF_2CF_3 , $C(Y^3)_2C(Y^3)_3$, substituted alkenyl, haloalkenyl (but not Br-vinyl), substituted

alkynyl, haloalkynyl, optionally substituted carbocycle, optionally substituted heterocycle, optionally substituted heteroaryl, $-CH_2C(O)OH$, $-CH_2C(O)OR^4$, $-CH_2C(O)O$ (lower alkyl),

25 $-CH_2C(O)SH$, $-CH_2C(O)SR^4$, $-CH_2C(O)S$ (lower alkyl), $-CH_2C(O)NH_2$, $-CH_2C(O)NHR^4$,

$-CH_2C(O)NH$ (lower alkyl), $-CH_2C(O)N(R^4)_2$, $-CH_2C(O)N$ (lower alkyl) $_2$, $-(CH_2)_mC(O)OH$,

$-(CH_2)_mC(O)OR^4$, $-(CH_2)_mC(O)O$ (lower alkyl), $-(CH_2)_mC(O)SH$, $-(CH_2)_mC(O)SR^4$,

$-(CH_2)_mC(O)S$ (lower alkyl), $-(CH_2)_mC(O)NH_2$, $-(CH_2)_mC(O)NHR^4$, $-(CH_2)_mC(O)NH$ (lower alkyl),

$-(CH_2)_mC(O)N(R^4)_2$, $-(CH_2)_mC(O)N$ (lower alkyl) $_2$, $-C(O)OH$, $-C(O)OR^4$, $-C(O)SH$,

30 $-C(O)SR^4$, $-C(O)S$ (lower alkyl), $-C(O)NH_2$, $-C(O)NHR^4$, $-C(O)NH$ (lower alkyl),

$-C(O)N(R^4)_2$, $-C(O)N$ (lower alkyl) $_2$, $-O(R^4)$, $-O$ (alkynyl), $-O$ (aralkyl), $-O$ (cycloalkyl), $-$

S (acyl), $-S$ (lower acyl), $-S(R^4)$, $-S$ (lower alkyl), $-S$ (alkenyl), $-S$ (alkynyl), $-S$ (aralkyl),

$-S$ (cycloalkyl), $-NHR^4$, $-NR^4R^5$, $-NH$ (alkenyl), $-NH$ (alkynyl), $-NH$ (aralkyl),

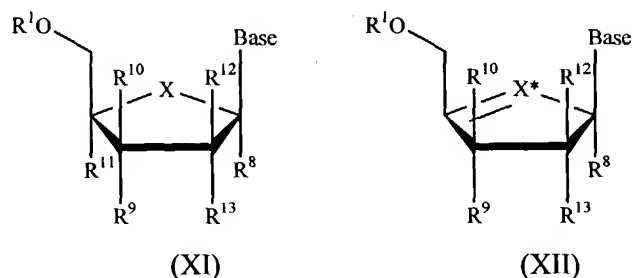
$-NH$ (cycloalkyl), SCN, OCN, NCO or fluoro;

alternatively, R^{12} and R^{13} can come together to form a spiro compound selected from the group consisting of optionally substituted carbocycle or optionally substituted heterocycle; and

each m is independently 0, 1 or 2.

5

6. A compound of Formula (XI) or (XII):



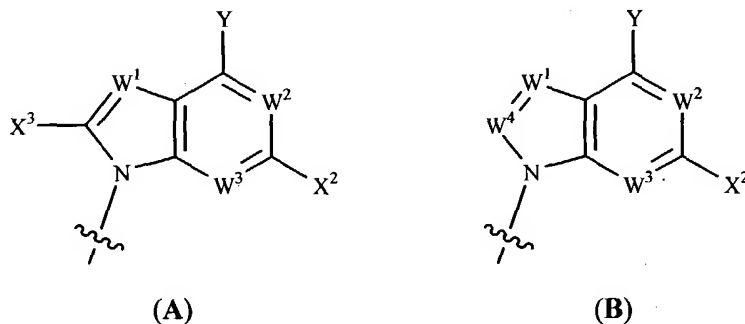
or a pharmaceutically acceptable salt thereof, wherein:

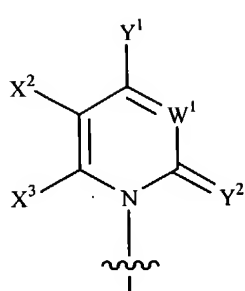
10

R^1 is H; phosphate; straight chained, branched or cyclic alkyl; acyl; CO-alkyl; CO-aryl; CO-alkoxyalkyl; CO-aryloxyalkyl; CO-substituted aryl; sulfonate ester; benzyl, wherein the phenyl group is optionally substituted with one or more substituents; alkylsulfonyl; arylsulfonyl; aralkylsulfonyl; a lipid; an amino acid; an amino acid residue; a carbohydrate; a peptide; cholesterol; or pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1 is H or phosphate;

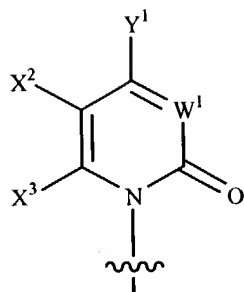
15

Base is selected from the group consisting of

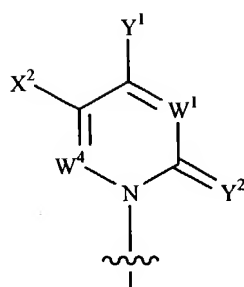




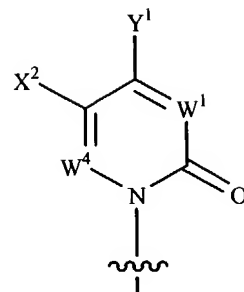
(C)



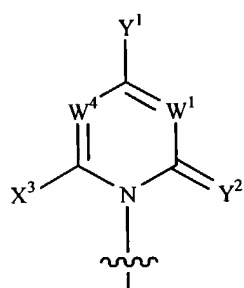
(D)



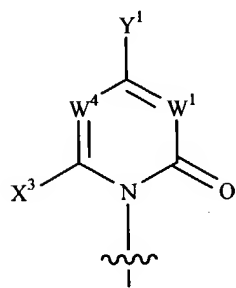
(E)



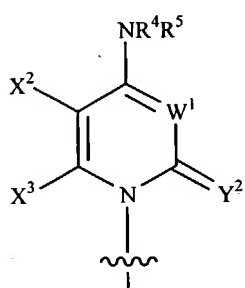
(F)



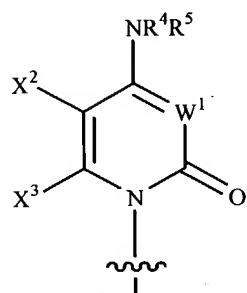
(G)



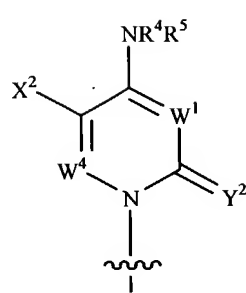
(H)



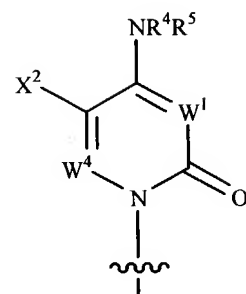
(I)



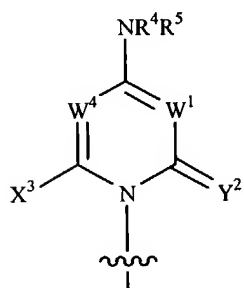
(J)



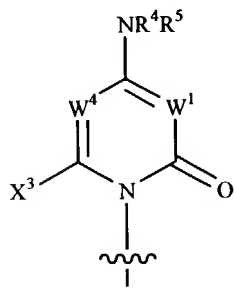
(K)



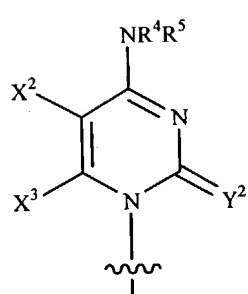
(L)



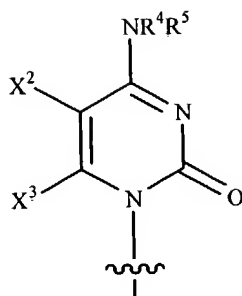
(M)



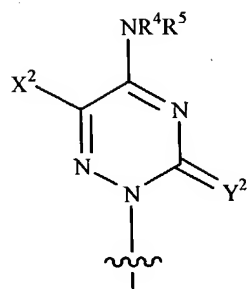
(N)



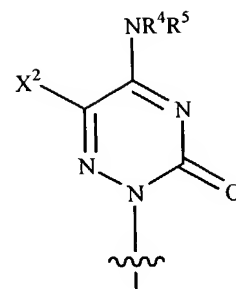
(O)



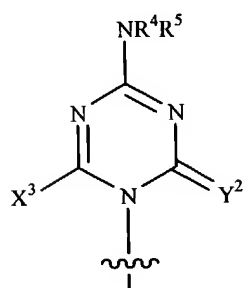
(P)



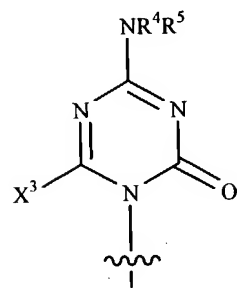
(Q)



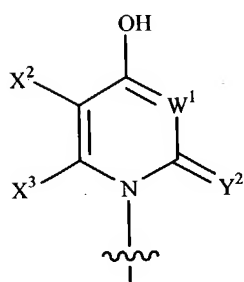
(R)



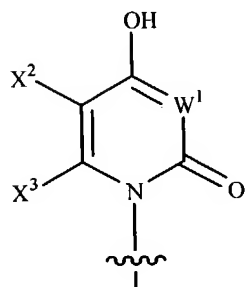
(S)



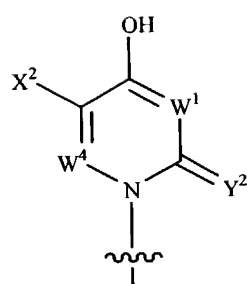
(T)



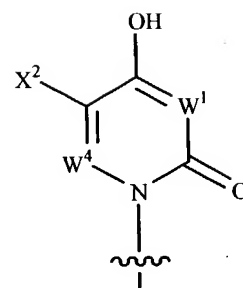
(U)



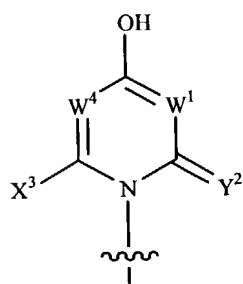
(V)



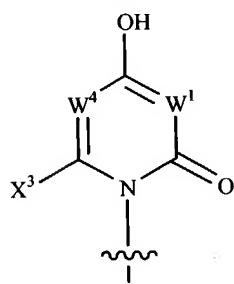
(W)



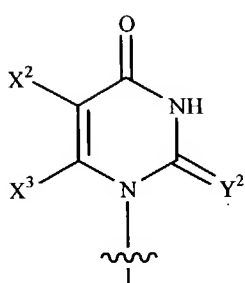
(X)



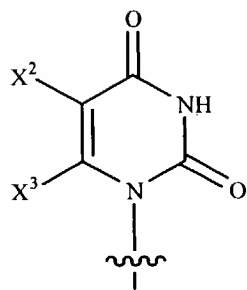
(Y)



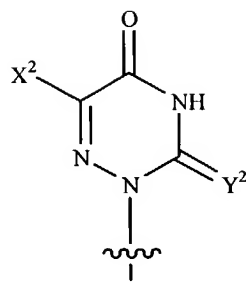
(Z)



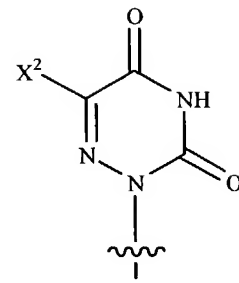
(AA)



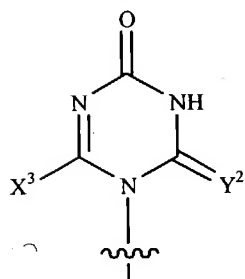
(AB)



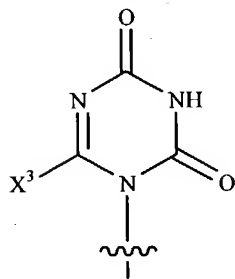
(AC)



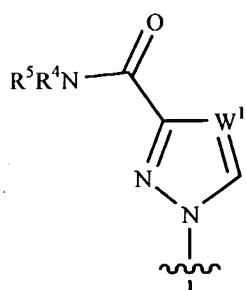
(AD)



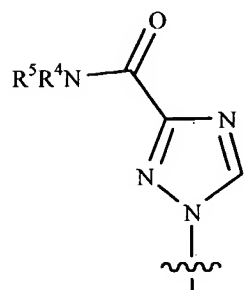
(AE)



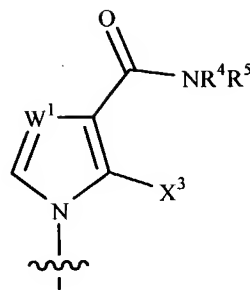
(AF)



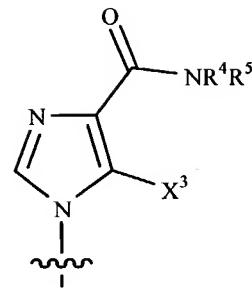
(AG)



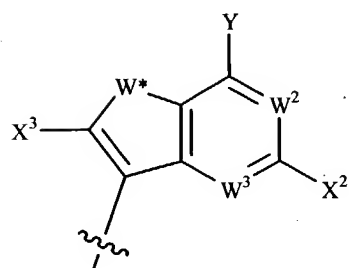
(AH)



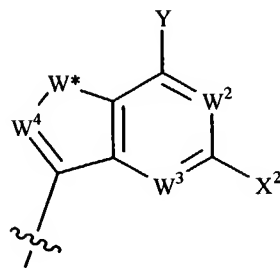
(AI)



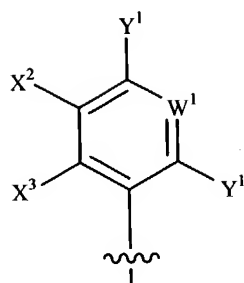
(AJ)



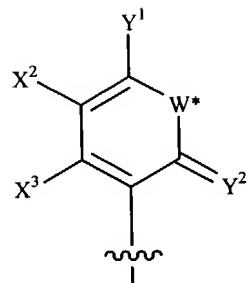
(BA)



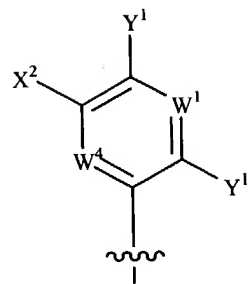
(BB)



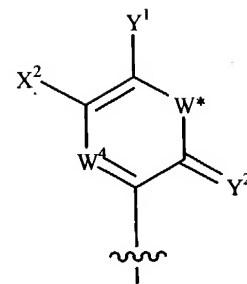
(BC)



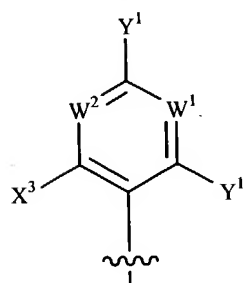
(BD)



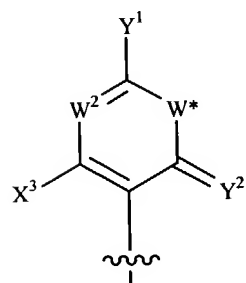
(BE)



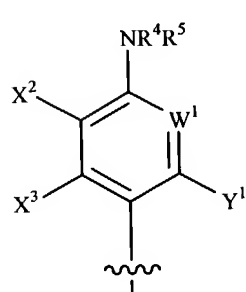
(BF)



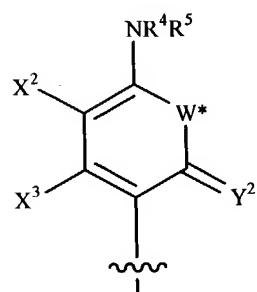
(BG)



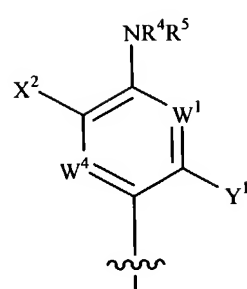
(BH)



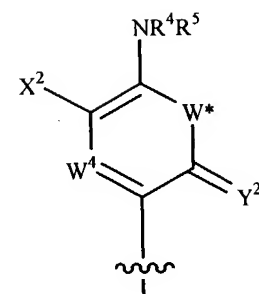
(BI)



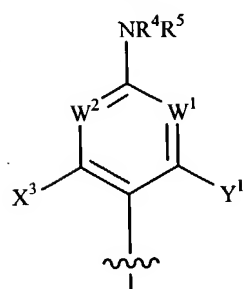
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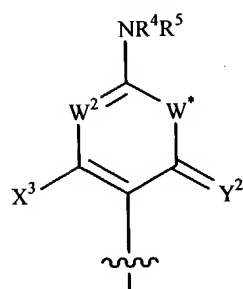
(BK)



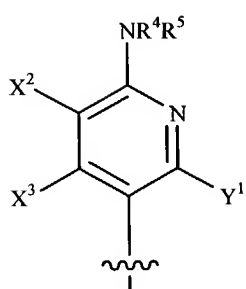
(BL)



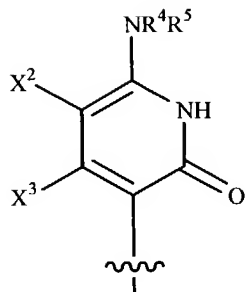
(BM)



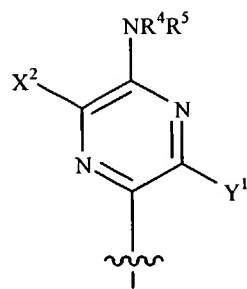
(BN)



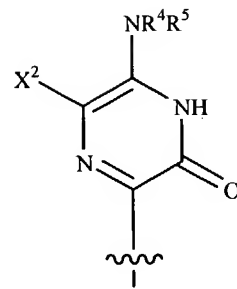
(BO)



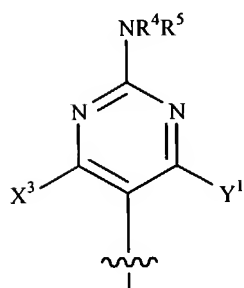
(BP)



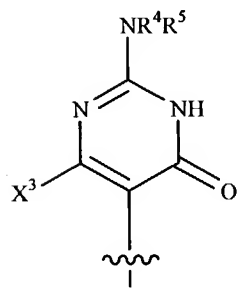
(BQ)



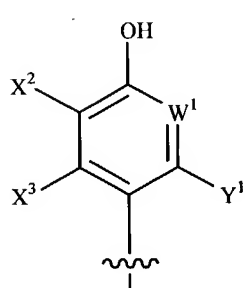
(BR)



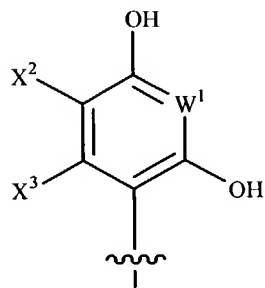
(BS)



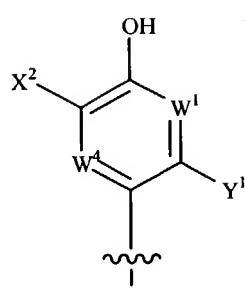
(BT)



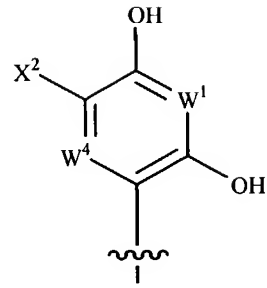
(BU)



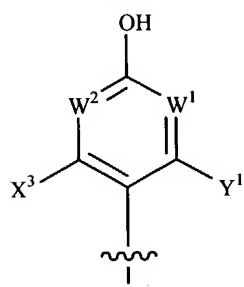
(BV)



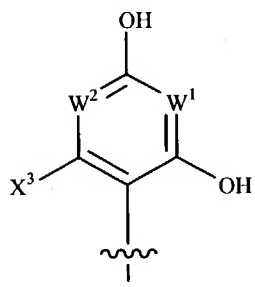
(BW)



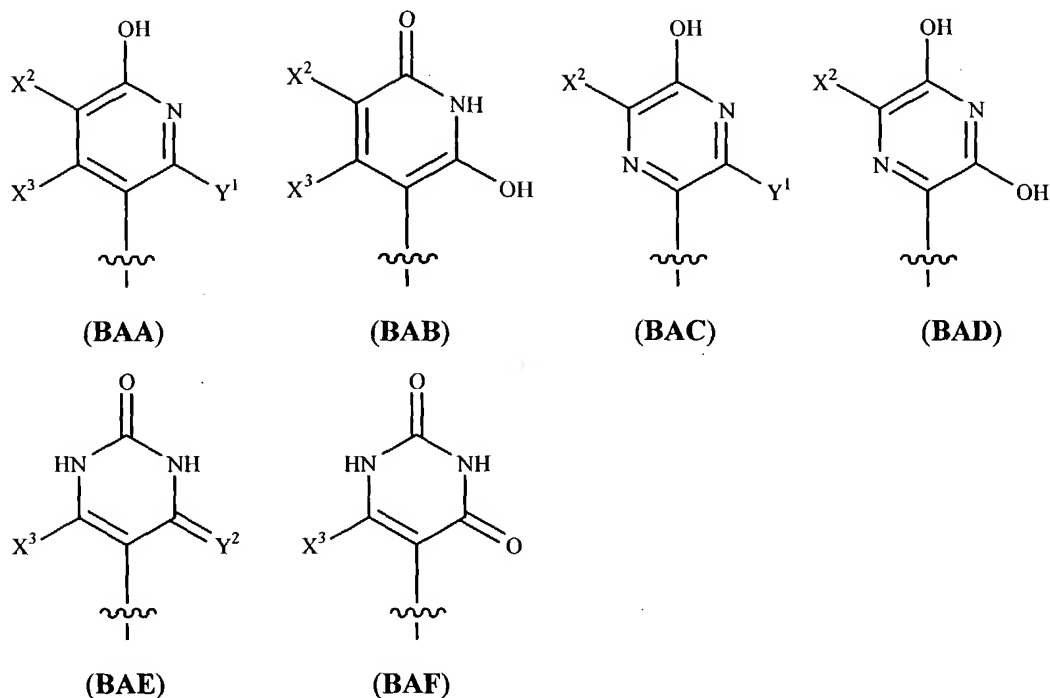
(BX)



(BY)



(BZ)



5

each W^1 , W^2 , W^3 and W^4 is independently N, CH, CF, Cl, CBr, CCl, CCN, CCH₃, CCF₃, CCH₂CH₃, CC(O)NH₂, CC(O)NHR⁴, CC(O)N(R⁴)₂, CC(O)OH, CC(O)OR⁴ or CX³;

each W^* is independently O, S, NH or NR⁴;

10 X is O, S, SO₂, CH₂, CH₂OH, CHF, CF₂, C(Y³)₂, CHCN, C(CN)₂, CHR⁴ or C(R⁴)₂;

X* is CH, CF, CY³ or CR⁴;

X² is H, straight chained, branched or cyclic optionally substituted alkyl, CH₃, CF₃, C(Y³)₃, 2-Br-ethyl, CH₂F, CH₂Cl, CH₂CF₃, CF₂CF₃, C(Y³)₂C(Y³)₃, CH₂OH, optionally substituted alkenyl, optionally substituted alkynyl, COOH, COOR⁴, COO-alkyl, COO-aryl, 15 CO-Oalkoxyalkyl, CONH₂, CONHR⁴, CON(R⁴)₂, chloro, bromo, fluoro, iodo, CN, N₃, OH, OR⁴, NH₂, NHR⁴, NR⁴R⁵, SH or SR⁵;

each X³ is independently a straight chained, branched or cyclic optionally substituted alkyl, CH₃, CH₂CN, CH₂N₃, CH₂NH₂, CH₂NHCH₃, CH₂N(CH₃)₂, CH₂OH, halogenated alkyl, CF₃, C(Y³)₃, 2-Br-ethyl, CH₂F, CH₂Cl, CH₂CF₃, CF₂CF₃, C(Y³)₂C(Y³)₃, 20 optionally substituted alkenyl, haloalkenyl, Br-vinyl, optionally substituted alkynyl, haloalkynyl, N₃, CN, -C(O)OH, -C(O)OR⁴, -C(O)O(lower alkyl), -C(O)NH₂, -C(O)NHR⁴, -C(O)NH(lower alkyl), -C(O)N(R⁴)₂, -C(O)N(lower alkyl)₂, OH, OR⁴, -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), -O(alkynyl), -O(aralkyl), -O(cycloalkyl), -

- S(acyl), -S(lower acyl), -S(R⁴), -S(lower alkyl), -S(alkenyl), -S(alkynyl), -S(aralkyl), -S(cycloalkyl), chloro, bromo, fluoro, iodo, NH₂, -NH(lower alkyl), -NHR⁴, -NR⁴R⁵, -NH(acyl), -N(lower alkyl)₂, -NH(alkenyl), -NH(alkynyl), -NH(aralkyl), -NH(cycloalkyl), or -N(acyl)₂;
- 5 each Y is independently selected from the group consisting of H, optionally substituted lower alkyl, cycloalkyl, alkenyl, alkynyl, CH₂OH, CH₂NH₂, CH₂NHCH₃, CH₂N(CH₃)₂, CH₂F, CH₂Cl, CH₂N₃, CH₂CN, CH₂CF₃, CF₃, CF₂CF₃, CH₂CO₂R, (CH₂)_mCOOH, (CH₂)_mCOOR, (CH₂)_mCONH₂, (CH₂)_mCONR₂, and (CH₂)_mCONHR;
- R is H, alkyl or acyl;
- 10 Y¹ is hydrogen, bromo, chloro, fluoro, iodo, CN, OH, OR⁴, NH₂, NHR⁴, NR⁴R⁵, SH or SR⁴;
- each Y² is independently O, S, NH or NR⁴;
- each Y³ is independently H, F, Cl, Br or I;
- wherein for Base (B), W⁴ cannot be CH if W¹, W² and W³ are N;
- 15 wherein for Base (E), (F), (K), (L), (W) and (X), W⁴ cannot be CH if W¹ is N;
- each R⁴ and R⁵ is independently hydrogen, acyl, alkyl, lower alkyl, alkenyl, alkynyl or cycloalkyl;
- each R¹² is independently a substituted alkyl, CH₂CN, CH₂N₃, CH₂NH₂, CH₂NHCH₃, CH₂N(CH₃)₂, CH₂OH, halogenated alkyl, CF₃, C(Y³)₃, 2-Br-ethyl, CH₂F, CH₂Cl, CH₂CF₃, CF₂CF₃, C(Y³)₂C(Y³)₃, substituted alkenyl, haloalkenyl (but not Br-vinyl), substituted alkynyl, haloalkynyl, -CH₂C(O)OH, -CH₂C(O)OR⁴, -CH₂C(O)O(lower alkyl), -CH₂C(O)NH₂, -CH₂C(O)NHR⁴, -CH₂C(O)NH(lower alkyl), -CH₂C(O)N(R⁴)₂, -CH₂C(O)N(lower alkyl)₂, -(CH₂)_mC(O)OH, -(CH₂)_mC(O)OR⁴, -(CH₂)_mC(O)O(lower alkyl), -(CH₂)_mC(O)NH₂, -(CH₂)_mC(O)NHR⁴, -(CH₂)_mC(O)NH(lower alkyl), -(CH₂)_mC(O)N(R⁴)₂, -(CH₂)_mC(O)N(lower alkyl)₂, -C(O)OH, -C(O)OR⁴, -C(O)NH₂, -C(O)NHR⁴, -C(O)NH(lower alkyl), or -C(O)N(R⁴)₂, -C(O)N(lower alkyl)₂;
- 20 each R¹³ is independently substituted alkyl, CH₂CN, CH₂N₃, CH₂NH₂, CH₂NHCH₃, CH₂N(CH₃)₂, CH₂OH, halogenated alkyl (including halogenated lower alkyl), CF₃, C(Y³)₃, 2-Br-ethyl, CH₂F, CH₂Cl, CH₂CF₃, CF₂CF₃, C(Y³)₂C(Y³)₃, substituted alkenyl, haloalkenyl (but not Br-vinyl), substituted alkynyl, haloalkynyl, optionally substituted carbocycle, optionally substituted heterocycle, optionally substituted heteroaryl, -CH₂C(O)OH, -CH₂C(O)OR⁴, -CH₂C(O)O(lower alkyl), -CH₂C(O)SH, -CH₂C(O)SR⁴, -CH₂C(O)S(lower alkyl), -CH₂C(O)NH₂, -CH₂C(O)NHR⁴, -CH₂C(O)NH(lower alkyl), -CH₂C(O)N(R⁴)₂, -CH₂C(O)N(lower alkyl)₂, -(CH₂)_mC(O)OH, -(CH₂)_mC(O)OR⁴, -(CH₂)_mC(O)O(lower
- 25
- 30

alkyl), $-(CH_2)_mC(O)SH$, $-(CH_2)_mC(O)SR^4$, $-(CH_2)_mC(O)S(\text{lower alkyl})$, $-(CH_2)_mC(O)NH_2$,
 $-(CH_2)_mC(O)NHR^4$, $-(CH_2)_mC(O)NH(\text{lower alkyl})$, $-(CH_2)_mC(O)N(R^4)_2$,
 $-(CH_2)_mC(O)N(\text{lower alkyl})_2$, $-C(O)OH$, $-C(O)OR^4$, $-C(O)SH$, $-C(O)SR^4$, $-C(O)S(\text{lower alkyl})$,
 $-C(O)NH_2$, $-C(O)NHR^4$, $-C(O)NH(\text{lower alkyl})$, $-C(O)N(R^4)_2$, $-C(O)N(\text{lower alkyl})_2$,
5 $-O(R^4)$, $-O(\text{alkynyl})$, $-O(\text{aralkyl})$, $-O(\text{cycloalkyl})$, $-S(\text{acyl})$, $-S(\text{lower acyl})$, $-S(R^4)$, $-S(\text{lower alkyl})$,
 $-S(\text{alkenyl})$, $-S(\text{alkynyl})$, $-S(\text{aralkyl})$, $-S(\text{cycloalkyl})$, $-NHR^4$, $-NR^4R^5$, $-NH(\text{alkenyl})$,
 $-NH(\text{alkynyl})$, $-NH(\text{aralkyl})$, $-NH(\text{cycloalkyl})$, SCN , OCN , NCO or fluoro; and

alternatively, R^{12} and R^{13} can come together to form a spiro compound selected from
the group consisting of optionally substituted carbocycle or optionally substituted
10 heterocycle;

each R^8 and R^{11} is independently hydrogen, an optionally substituted alkyl
(including lower alkyl), CH_3 , CH_2CN , CH_2N_3 , CH_2NH_2 , CH_2NHCH_3 , $CH_2N(CH_3)_2$,
 CH_2OH , halogenated alkyl (including halogenated lower alkyl), CF_3 , $C(Y^3)_3$, 2-Br-ethyl,
 CH_2F , CH_2Cl , CH_2CF_3 , CF_2CF_3 , $C(Y^3)_2C(Y^3)_3$, optionally substituted alkenyl, haloalkenyl,
15 Br-vinyl, optionally substituted alkynyl, haloalkynyl, $-CH_2C(O)OH$, $-CH_2C(O)OR^4$,
 $-CH_2C(O)O(\text{lower alkyl})$, $-CH_2C(O)NH_2$, $-CH_2C(O)NHR^4$, $-CH_2C(O)NH(\text{lower alkyl})$,
 $-CH_2C(O)N(R^4)_2$, $-CH_2C(O)N(\text{lower alkyl})_2$, $-(CH_2)_mC(O)OH$, $-(CH_2)_mC(O)OR^4$,
 $-(CH_2)_mC(O)O(\text{lower alkyl})$, $-(CH_2)_mC(O)NH_2$, $-(CH_2)_mC(O)NHR^4$, $-(CH_2)_mC(O)NH(\text{lower alkyl})$,
 $-(CH_2)_mC(O)N(R^4)_2$, $-(CH_2)_mC(O)N(\text{lower alkyl})_2$, $-C(O)OH$, $-C(O)OR^4$,
20 $-C(O)O(\text{lower alkyl})$, $-C(O)NH_2$, $-C(O)NHR^4$, $-C(O)NH(\text{lower alkyl})$, $-C(O)N(R^4)_2$,
 $-C(O)N(\text{lower alkyl})_2$, cyano, NH-acyl or N(acyl)₂;

each R^9 and R^{10} are independently hydrogen, OH, OR^2 , optionally substituted alkyl,
 CH_3 , CH_2CN , CH_2N_3 , CH_2NH_2 , CH_2NHCH_3 , $CH_2N(CH_3)_2$, CH_2OH , halogenated alkyl,
 CF_3 , $C(Y^3)_3$, 2-Br-ethyl, CH_2F , CH_2Cl , CH_2CF_3 , CF_2CF_3 , $C(Y^3)_2C(Y^3)_3$, optionally
25 substituted alkenyl, haloalkenyl, Br-vinyl, optionally substituted alkynyl, haloalkynyl,
optionally substituted carbocycle, optionally substituted heterocycle, optionally substituted
heteroaryl, $-CH_2C(O)OH$, $-CH_2C(O)OR^4$, $-CH_2C(O)O(\text{lower alkyl})$, $-CH_2C(O)SH$,
 $-CH_2C(O)SR^4$, $-CH_2C(O)S(\text{lower alkyl})$, $-CH_2C(O)NH_2$, $-CH_2C(O)NHR^4$,
 $-CH_2C(O)NH(\text{lower alkyl})$, $-CH_2C(O)N(R^4)_2$, $-CH_2C(O)N(\text{lower alkyl})_2$, $-(CH_2)_mC(O)OH$,
30 $-(CH_2)_mC(O)OR^4$, $-(CH_2)_mC(O)O(\text{lower alkyl})$, $-(CH_2)_mC(O)SH$, $-(CH_2)_mC(O)SR^4$,
 $-(CH_2)_mC(O)S(\text{lower alkyl})$, $-(CH_2)_mC(O)NH_2$, $-(CH_2)_mC(O)NHR^4$, $-(CH_2)_mC(O)NH(\text{lower alkyl})$,
 $-(CH_2)_mC(O)N(R^4)_2$, $-(CH_2)_mC(O)N(\text{lower alkyl})_2$, $-C(O)OH$, $-C(O)OR^4$,
 $-C(O)O(\text{lower alkyl})$, $-C(O)SH$, $-C(O)SR^4$, $-C(O)S(\text{lower alkyl})$, $-C(O)NH_2$, $-C(O)NHR^4$,
 $-C(O)NH(\text{lower alkyl})$, $-C(O)N(R^4)_2$, $-C(O)N(\text{lower alkyl})_2$, $-O(\text{acyl})$, $-O(\text{lower acyl})$,

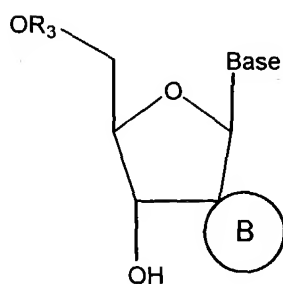
-O(R⁴), -O(alkyl), -O(lower alkyl), -O(alkenyl), -O(alkynyl), -O(aralkyl), -O(cycloalkyl), -S(acyl), -S(lower acyl), -S(R⁴), -S(lower alkyl), -S(alkenyl), -S(alkynyl), -S(aralkyl), -S(cycloalkyl), NO₂, NH₂, -NH(lower alkyl), -NHR⁴, -NR⁴R⁵, -NH(acyl), -N(lower alkyl)₂, -NH(alkenyl), -NH(alkynyl), -NH(aralkyl), -NH(cycloalkyl), -N(acyl)₂, azido, cyano, SCN, OCN, NCO or halo;

each m is independently 0, 1 or 2; and

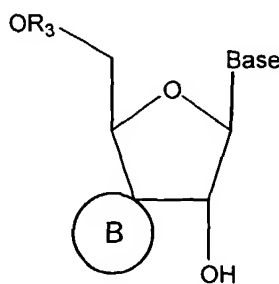
alternatively, R⁸ and R¹³, R⁹ and R¹³, R⁹ and R¹¹ or R¹⁰ and R¹² can come together to form a bridged compound selected from the group consisting of optionally substituted carbocycle or optionally substituted heterocycle; or

alternatively, R¹² and R¹³ or R⁹ and R¹⁰ can come together to form a spiro compound selected from the group consisting of optionally substituted or optionally substituted heterocycle.

7. A compound of the Formula (XIII) or (XIV):



(XIII)



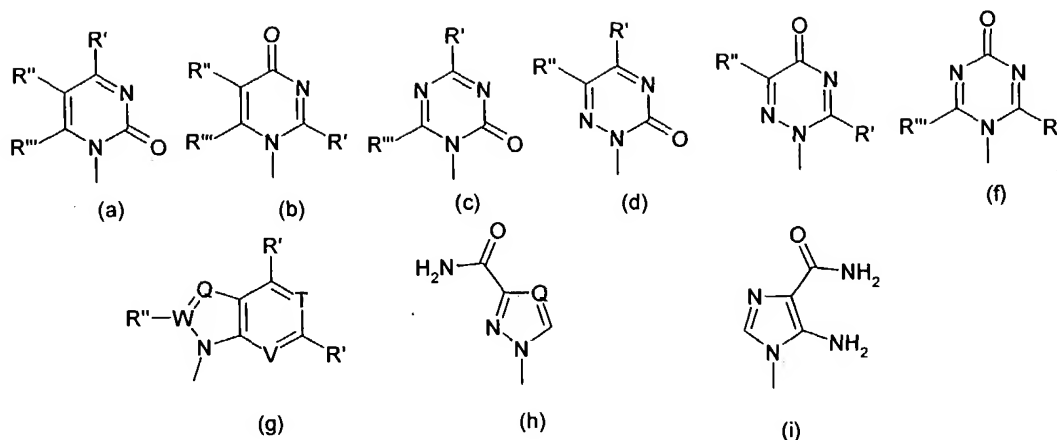
(XIV)

or a pharmaceutically acceptable salt thereof, wherein:

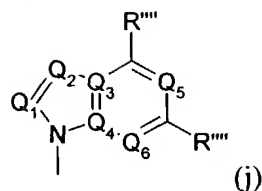
R₃ is selected from the group consisting of H; mono-, di-, and tri-phosphate or a stabilized phosphate prodrug; acyl; a sulfonate ester; optionally substituted alkyl sulfonyl; optionally substituted arylsulfonyl; a lipid; an amino acid; a carbohydrate; a peptide; cholesterol; and a pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R₃ is independently H, or mono-, di- or triphosphate;

B indicates a spiro compound selected from the group consisting of optionally substituted carbocycle or optionally substituted heterocycle;

Base is selected from the group consisting of:



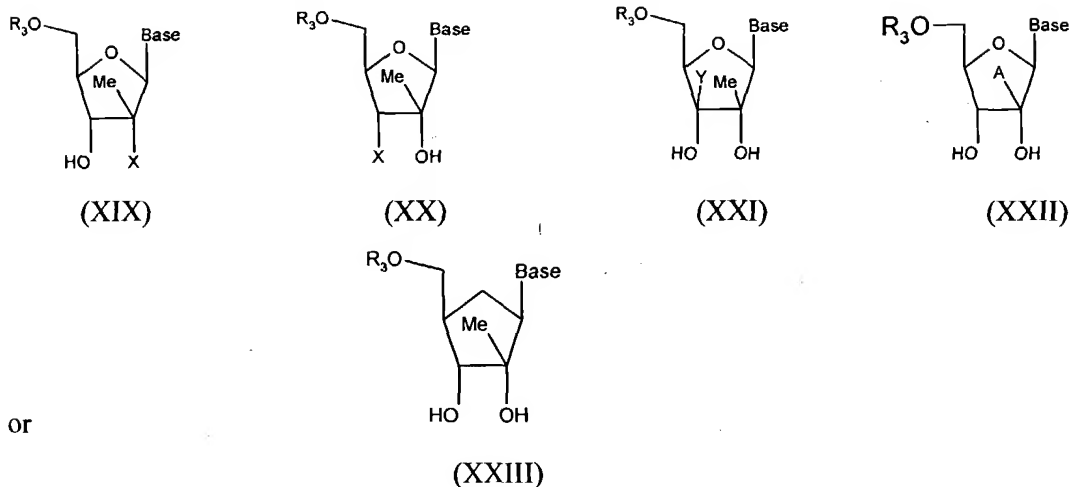
and



wherein

- 5 each R', R'', R''' and R'''' are independently selected from the group consisting of H, OH, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, cycloalkyl, Br-vinyl, -O-alkyl, O-alkenyl, O-alkynyl, O-aryl, O-aralkyl, -O-acyl, O-cycloalkyl, NH₂, NH-alkyl, N-dialkyl, NH-acyl, N-aryl, N-aralkyl, NH-cycloalkyl, SH, S-alkyl, S-acyl, S-aryl, S-cycloalkyl, S-aralkyl, F, Cl, Br, I, CN, COOH, CONH₂, CO₂-alkyl, CONH-alkyl, CON-dialkyl, OH, CF₃, CH₂OH, (CH₂)_mOH, (CH₂)_mNH₂, (CH₂)_mCOOH, (CH₂)_mCN, (CH₂)_mNO₂ and (CH₂)_mCONH₂;
- 10 m is 0 or 1;
- W is C-R'' or N;
- 15 T and V independently are CH or N;
- Q is CH, -CCl, -CBr, -CF, -Cl, -CCN, -C-COOH, -C-CONH₂, or N;
- Q₁ and Q₂ independently are N or C-R;
- R is H, alkyl, or acyl; and
- 20 Q₃, Q₄, Q₅ and Q₆ independently are N or CH.

8. A compound of Formula (XIX), (XX), (XXI) (XXII) or (XXIII):



or a pharmaceutically acceptable salt thereof, wherein:

A is selected from the group consisting of optionally substituted lower alkyl, cycloalkyl, alkenyl, alkynyl, CH_2OH , CH_2NH_2 , CH_2NHCH_3 , $\text{CH}_2\text{N}(\text{CH}_3)_2$, CH_2F , CH_2Cl , CH_2N_3 , CH_2CN , CH_2CF_3 , CF_3 , CF_2CF_3 , $\text{CH}_2\text{CO}_2\text{R}$, $(\text{CH}_2)_m\text{COOH}$, $(\text{CH}_2)_m\text{COOR}$, $(\text{CH}_2)_m\text{CONH}_2$, $(\text{CH}_2)_m\text{CONR}_2$, and $(\text{CH}_2)_m\text{CONHR}$;

Y is selected from the group consisting of H, optionally substituted lower alkyl, cycloalkyl, alkenyl, alkynyl, CH_2OH , CH_2NH_2 , CH_2NHCH_3 , $\text{CH}_2\text{N}(\text{CH}_3)_2$, CH_2F , CH_2Cl , CH_2N_3 , CH_2CN , CH_2CF_3 , CF_3 , CF_2CF_3 , $\text{CH}_2\text{CO}_2\text{R}$, $(\text{CH}_2)_m\text{COOH}$, $(\text{CH}_2)_m\text{COOR}$, $(\text{CH}_2)_m\text{CONH}_2$, $(\text{CH}_2)_m\text{CONR}_2$, and $(\text{CH}_2)_m\text{CONHR}$;

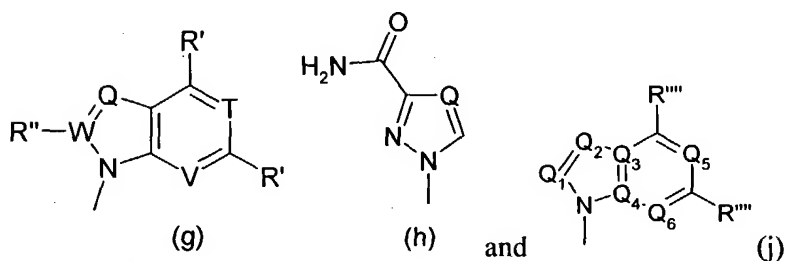
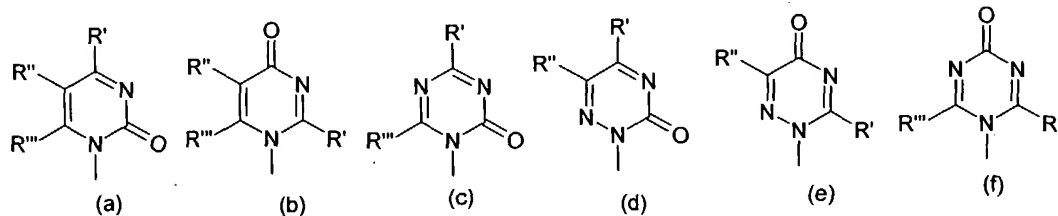
R is H, alkyl or acyl;

X is selected from the group consisting of -OH, optionally substituted alkyl, cycloalkyl, alkenyl, alkynyl, -O-alkyl, -O-alkenyl, -O-alkynyl, -O-aryl, -O-aralkyl, -O-cycloalkyl-, O-acyl, F, Cl, Br, I, CN, NC, SCN, OCN, NCO, NO_2 , NH_2 , N_3 , NH-acyl, NH-alkyl, N-dialkyl, NH-alkenyl, NH-alkynyl, NH-aryl, NH-aralkyl, NH-cycloalkyl, SH, S-alkyl, S-alkenyl, S-alkynyl, S-aryl, S-aralkyl, S-acyl, S-cycloalkyl, CO_2 -alkyl, CONH-alkyl, CON-dialkyl, CONH-alkenyl, CONH-alkynyl, CONH-aralkyl, CONH-cycloalkyl, CH_2OH , CH_2NH_2 , CH_2NHCH_3 , $\text{CH}_2\text{N}(\text{CH}_3)_2$, CH_2F , CH_2Cl , CH_2N_3 , CH_2CN , CH_2CF_3 , CF_3 , CF_2CF_3 , $\text{CH}_2\text{CO}_2\text{R}$, $(\text{CH}_2)_m\text{COOH}$, $(\text{CH}_2)_m\text{COOR}$, $(\text{CH}_2)_m\text{CONH}_2$, $(\text{CH}_2)_m\text{CONR}_2$, $(\text{CH}_2)_m\text{CONHR}$, an optionally substituted 3-7 membered carbocyclic, and an optionally substituted 3-7 membered heterocyclic ring having O, S and/or N independently as a heteroatom taken alone or in combination;

m is 0 or 1;

R_3 is selected from the group consisting of H; mono-, di-, and tri-phosphate or a stabilized phosphate prodrug; substituted or unsubstituted alkyl; acyl; a sulfonate ester; optionally substituted alkyl sulfonyl; optionally substituted arylsulfonyl; a lipid; an amino acid; a carbohydrate; a peptide; cholesterol; and a pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R_3 is independently H, or mono-, di- or triphosphate; and

Base is a non-natural base selected from the group of:



wherein:

each R' , R'' , R''' and R'''' is independently selected from the group consisting of H, OH, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, cycloalkyl, Br-vinyl, -O-alkyl, O-alkenyl, O-alkynyl, O-aryl, O-aralkyl, -O-acyl, O-cycloalkyl, NH_2 , NH-alkyl, N-dialkyl, NH-acyl, N-aryl, N-aralkyl, NH-cycloalkyl, SH, S-alkyl, S-acyl, S-aryl, S-cycloalkyl, S-aralkyl, F, Cl, Br, I, CN, COOH, $CONH_2$, CO_2 -alkyl, CONH-alkyl, CON-dialkyl, OH, CF_3 , CH_2OH , $(CH_2)_mOH$, $(CH_2)_mNH_2$, $(CH_2)_mCOOH$, $(CH_2)_mCN$, $(CH_2)_mNO_2$ and $(CH_2)_mCONH_2$;

m is 0 or 1;

W is C- R'' or N;

T and V independently are CH or N;

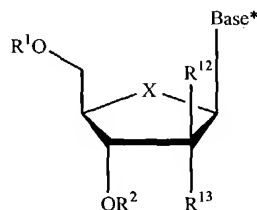
Q is CH, -CCl, -CBr, -CF, -Cl, -CCN, -C-COOH, -C- $CONH_2$, or N;

Q_1 and Q_2 independently are N or C- R'''' ; and

Q_3 , Q_4 , Q_5 and Q_6 independently are N or CH;

with the proviso that in bases (g) and (i), R', R''' are not H, OH, or NH₂; and Q, T, V, Q₂, Q₅ and Q₆ are not N.

9. A compound of Formula (IX):



(IX)

or a pharmaceutically acceptable salt thereof, wherein:

R¹, R² and R³ are independently H; phosphate; straight chained, branched or cyclic alkyl; acyl; CO-alkyl; CO-aryl; CO-alkoxyalkyl; CO-aryloxyalkyl; CO-substituted aryl; sulfonate ester; benzyl, wherein the phenyl group is optionally substituted with one or more substituents; alkylsulfonyl; arylsulfonyl; aralkylsulfonyl; a lipid; an amino acid; a carbohydrate; a peptide; cholesterol; or a pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R¹, R² and/or R³ is independently H or phosphate;

X is O, S, SO₂ or CH₂;

Base* is a purine or pyrimidine base;

R¹² is C(Y³)₃;

Y³ is independently H, F, Cl, Br or I; and

R¹³ is fluoro.

10. The compound of claim 9, wherein X is O, and Y³ is H.

11. The compound of claim 10, wherein R¹, R² and R³ are H.

12. A method for the treatment of a host infected with a *Flaviviridae* virus, comprising administering an effective treatment amount of a compound as claimed in any one of claims 1-11, or a pharmaceutically acceptable salt thereof.

13. The method of claim 12, wherein the virus is hepatitis C.

14. The method of claim 12, wherein the compound or pharmaceutically acceptable salt thereof is administered in combination or alternation with a second anti-viral agent.

5 15. The method of claim 14, wherein the second anti-viral agent is selected from the group consisting of an interferon, a ribavirin, an interleukin, a NS3 protease inhibitor, a cysteine protease inhibitor, a phenan-threnequinone, a thiazolidine derivative, a thiazolidine, a benzanilide, a phenan-threnequinone, a helicase inhibitor, a polymerase inhibitor, a nucleotide analogue, a gliotoxin, a cerulenin, an antisense phosphorothioate
10 oligodeoxynucleotide, an inhibitor of IRES-dependent translation, and a ribozyme.

16. The method of claim 15, wherein the second anti-viral agent is an interferon.

15 17. The method of claim 16, wherein the second anti-viral agent is selected from the group consisting of pegylated interferon alpha 2a, interferon alphacon-1, natural interferon, albuferon, interferon beta-1a, omega interferon, interferon alpha, interferon gamma, interferon tau, interferon delta and interferon gamma- 1b.

20 18. The method of claim 12, wherein the compound or pharmaceutically acceptable salt thereof is in the form of a dosage unit.

19. The method of claim 18 wherein the dosage unit contains 50 to 1000 mg or 0.1 to 50 mg of the compound.

25 20. The method of claim 18 wherein the dosage unit is a tablet or capsule.

21. The method of claim 12, wherein the host is a human.

30 22. The method of claim 12, wherein the compound or pharmaceutically acceptable salt thereof is in substantially pure form.

23. The method of claim 12, wherein the compound or pharmaceutically acceptable salt thereof is at least 90% by weight of the β -D-isomer.

24. The method of claim 12, wherein the compound or pharmaceutically acceptable salt thereof is at least 95% by weight of the β -D-isomer.

25. The method of claim 12, wherein the compound is in the form of a pharmaceutically acceptable salt selected from the group consisting of a tosylate, methanesulfonate, acetate, citrate, malonate, tartarate, succinate, benzoate, ascorate, α -ketoglutarate, α -glycerophosphate, formate, fumarate, propionate, glycolate, lactate, pyruvate, oxalate, maleate, salicylate, sulfate, nitrate, bicarbonate, carbonate salts, hydrobromate, hydrochloride, di-hydrochloride, and phosphoric acid salt.

26. The method of claim 25, wherein the pharmaceutically acceptable salt is a hydrochloride salt.

27. A pharmaceutical composition comprising an effective amount to treat a *Flaviviridae* infection of a compound, or a pharmaceutically acceptable salt thereof, of any of claims 1 to 11 in a pharmaceutically acceptable carrier .

28. The pharmaceutical composition of claim 27, wherein the carrier is suitable for oral delivery.

29. The pharmaceutical composition of claim 27 comprising an effective amount of the compound or pharmaceutically acceptable salt thereof to treat a host infected with West Nile Virus, Yellow fever, Denge Virus or BVDV.

30. The composition of claim 27, wherein the *Flaviviridae* virus is hepatitis C.

31. The pharmaceutical composition of claim 29, wherein the compound or pharmaceutically acceptable salt thereof, is in the form of a dosage unit.

32. The composition of claim 31, wherein the dosage unit contains 0.1 to 50 mg or 50 to 1000 mg of the compound or pharmaceutically acceptable salt thereof.

33. The composition of claim 31, wherein said dosage unit is a tablet or capsule.

34. The pharmaceutical composition of claim 27, further comprising a second anti-viral agent.

5 35. The pharmaceutical composition of claim 34, wherein the second anti-viral agent is selected from the group consisting of an interferon, a ribavirin, an interleukin, a NS3 protease inhibitor, a cysteine protease inhibitor, a phenan-threnequinone, a thiazolidine derivative, a thiazolidine, a benzanilide, a phenan-threnequinone, a helicase inhibitor, a polymerase inhibitor, a nucleotide analogue, a gliotoxin, a cerulenin, an antisense phosphorothioate oligodeoxynucleotide, an inhibitor of IRES-dependent translation, and a
10 ribozyme.

36. The pharmaceutical composition of claim 35, wherein the second anti-viral agent is an interferon.

15 37. The pharmaceutical composition of claim 36, wherein the second anti-viral agent is selected from the group consisting of pegylated interferon alpha 2a, interferon alphacon-1, natural interferon, albuferon, interferon beta-1a, omega interferon, interferon alpha, interferon gamma, interferon tau, interferon delta and interferon gamma- 1b.

20 38. The pharmaceutical composition of claim 27, wherein the compound or pharmaceutically acceptable salt thereof, is in substantially pure form.

39. The pharmaceutical composition of claim 27, wherein the compound or pharmaceutically acceptable salt thereof, is at least 90% by weight of the β -D-isomer.
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40. The pharmaceutical composition of claim 27, wherein the compound or pharmaceutically acceptable salt thereof, is at least 95% by weight of the β -D-isomer.

41. The pharmaceutical composition of claim 27 further comprising a
30 pharmaceutically acceptable carrier suitable for oral, parenteral, inhalant or intravenous delivery.

42. The pharmaceutical composition of claim 27, wherein the pharmaceutically acceptable salt is selected from the group consisting of a tosylate, methanesulfonate, acetate,

citrate, malonate, tartarate, succinate, benzoate, ascorate, α -ketoglutarate, α -glycerophosphate, formate, fumarate, propionate, glycolate, lactate, pyruvate, oxalate, maleate, salicylate, sulfate, nitrate, bicarbonate, carbonate salts, hydrobromate, hydrochloride, di-hydrochloride, and phosphoric acid salt.

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43. The pharmaceutical composition of claim 42, wherein the pharmaceutically acceptable salt is a hydrochloride salt.

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